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AND THE ALLIED SCIENCES

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THE AMERICAN
JOURNAL OF PHARMACY

OCTOBER, 1920

EDITORIAL.

COMPREHENSIVE PHARMACEUTICAL RESEARCH.

One of the great lessons taught by the world war was the dependence of the industries upon the sciences. The tide of battle was swayed by the preponderance of scientific knowledge and its skillful application to the destruction of life and property. The destiny of nations was jeopardized and wavered in the balance until this advantage of the enemy became fully recognized and with feverish haste the latent resources, the inventive ingenuity and scientific knowledge of the allies, were mobilized into coördinated research.

The National Research Council was hastily organized in 1916 for the purpose of stimulating and coördinating research necessitated by the war problems and for a period this had the financial support of the National Government. In 1918, by executive order of the President of the United States, it was reorganized as a permanent body and the secretary now states that "its essential purpose is the promotion of scientific research and of the application and dissemination of scientific knowledge for the benefit of the national strength and well being."

While the conduct of the war to a favorable conclusion was pending as the largest contract ever undertaken by this nation, research as applied to the problems of the war, necessarily from the very urgency, received paramount consideration and held a prominent position in the public view. The value of scientific research appeared to be indelibly impressed upon government officials and many public spirited citizens. Now that the problems of war no longer hold the pre-eminent position in the public interest, it is in order to note how deep and how lasting have been the impressions made by this great lesson growing out of the exigencies of the war.

The National Research Council, we are advised, "is no longer government supported and while maintaining a close coöperation with the government scientific bureaus, it is in no sense a government bureau but is now entirely supported by other than government sources, and is entirely controlled by its own representatively selected membership and democratically chosen officers." The problems of peace are no less important than are those of war. The application of scientific principles to the development of the peaceful arts and industries assures a great increase in the productiveness, efficiency and wealth of the Nation and a larger measure of comfort and enjoyment to the individual. This means higher ideals in literature, art, industry and commerce, in fact in all proper lines of human effort, and far more toward the world's progress and happiness than can ever come from the destruction, devastation, destitution and misery resulting from the dire necessities of war.

The world has had its surfeit of war with the profligate waste of life and property. The time has now come for the inauguration of grand national movements by which scientific investigations shall be thoroughly and systematically organized and coördinated and the results obtained be applied intensely to the benefit of mankind. The conservation of our national resources and the stimulating of our industrial development in accordance with the highest scientific attainments, should now become our national problems. It is gratifying to observe that in England there has been established by government grant the Committee for Scientific and Industrial Research and in our own country that the National Research Council has been permanently reorganized and to note the efforts and the progress so far made by these movements.

Pharmacists are concerned that the necessity for the organization of a comprehensive plan for pharmaceutical research be recognized and that the value to mankind of the results that may be obtained thereby, shall be fully appreciated. So far the importance of the drug industry has not been publicly understood, and the insufficiency of our knowledge concerning nearly every potent medicine dispensed by pharmacists has not been given the consideration that is due either by the government authorities or by the philanthropists who have created research endowments or by those subsequently in control of such establishments. It is only too evident, that neither of these two national research foundations has yet given the serious consideration to the formulating of a plan for comprehensive phar-

maceutical research that, we are convinced, is merited by the importance of the subject and its benefit to the national strength and well being.

It is known that the National Research Council has named as one of its divisions "the medical sciences," but we are not advised that pharmacy is to be organized as a subdivision thereof or that pharmaceutical research is to be given special recognition or encouragement. We unhesitatingly assert that the thorough study of the numerous products supplied by pharmacists and the processes employed in the preparation of medicines, will open boundless fields for exploration with innumerable research problems the possibilities of which and the value thereof to mankind cannot be preestimated. We are firm in our conviction that "the sum of scientific knowledge for the benefit of the national strength and well being," acquired thereby will hold no secondary place.

Mr. W. Kirby, in his presidential address before the British Pharmaceutical Conference last year, fully set forth the need for pharmaceutical research and the duty of the government to encourage and foster this. At the recent meeting of the American Pharmaceutical Association, in responding to the address of Dr. C. E. McClung representing the Division of Medical Sciences of the National Research Council, Prof. John Uri Lloyd eloquently portrayed how the supplies of the pharmacist were drawn from every portion of the Natural Kingdoms and from all quarters of the globe and that these products alone presented an endless variety of problems of the utmost importance for investigation for the advancement of human knowledge to the benefit of mankind.

These representative leaders in pharmaceutic thought in their respective countries, comprehend fully the importance of comprehensive pharmaceutical research as a national asset and likewise its direct influence upon the development of professional pharmacy. If the entire membership of the pharmaceutical and drug trade organizations were imbued with the same spirit and comprehensive view of the subject, the internal indifference would give way to earnest, enthusiastic support and a national pharmaceutical research endowment would be promptly established and in its functioning maintain the proper professional status of pharmacy and demonstrate the sphere of usefulness of pharmacy to society and the service that it renders.

Pharmacy is not medicine nor is it chemistry, although closely

allied with each of these professions and coördinating with both in their respective spheres. It performs a distinct duty to the public and must be accorded recognition as a separate vocation with its own problems peculiar to its field of service. We cannot expect that the leader in medicine shall understand or that he will be especially concerned with the specific problems of pharmacy nor can we expect the chemist to have the viewpoint of the pharmacist. *It would be very unfortunate to all interests concerned to have pharmaceutical research controlled by others than pharmacists.* The propositions for pharmaceutic research that have heretofore emanated from these outside sources have but served to demonstrate the insufficiency of the view and the failure to comprehend the extensive fields awaiting organized pharmaceutical research. The plan of one of the proposed pharmaceutic research funds was limited to investigations of the pharmacologic actions of new synthetic chemicals for which therapeutic claims are made.

Any plan for pharmaceutical research that will have the hope of success must be a comprehensive scheme outlined by pharmacists who have a broad conception of the possibilities and a vision that will embrace every branch of pharmaceutical activity and coordinate the contemplated investigations with those of allied professions and industries. The acceptance of any other than a distinct and individual plan of research for pharmacy controlled and managed by pharmacists, must prove futile and wasteful of funds, time and energy. Pharmacy must energetically work out its own solution of the research question and incidentally its own destiny as the scientific progress and professional status of our vocation will depend in a large measure upon the manner in which this is done. In England as well as in the United States the importance of research is being recognized and there appears to be a growing sentiment that the pharmaceutical and drug trade organizations must form their own research association. Current literature amply demonstrates the need and the pages of the AMERICAN JOURNAL OF PHARMACY alone furnish numerous problems that call for further scientific investigation.

G. M. B.

RHUS VENENATA DC.

By Heber W. Youngken, Ph.D., and George A. Slothower, B.Sc. B.A.P.

PHILADELPHIA, PA.

Five poisonous species of Rhus plants are common to the United States and Canada, namely: *Rhus toxicodendron* L., *Rhus venenata* DC, *Rhus diversiloba* Torr. and Gray, *Rhus succedanea* L, and *Rhus vernicifera* DC.

Commercially, *Rhus vernicifera, Rhus succedanea,* and to some extent, *Rhus venenata,* yield a lac which is of value in the making of the famous Japan varnishes.

Rhus toxicodendron was official in the sixth and seventh editions of the U. S. P. Its use in medicine at the present time is in the main limited to the practice of homeopathy, where it is used in nervous disorders and dermatotherapy. Rost and Gilg[1] make mention of it as having been used in the treatment of cancer.

There are probably no other plants in existence which cause as much human distress and suffering as *Rhus toxicodendron* and *Rhus venenata.*

Many substances are referred to in the literature as causing the dermatitis produced by these plants. They include a vapor, gas, volatile alkaloid, volatile acid, infection by bacteria, glucoside, non-volatile acid, resin, polyhydric phenol and a non-volatile oil.

That the poisonous substance was a non-volatile oil, which resinifies on exposure to the atmopshere, was discovered by Pfaff[2] who found it to exist in all parts of the plant.

As to how this non-volatile oil comes in contact with individuals, the consensus of opinion seems to be that the winds and domestic animals carry the pollen grains and hairs. Pfaff and Schwalbe[3] found the pollen grains and hairs to contain the poisonous substance. On the other hand, Rost and Gilg,[1] in a very extensive work, were unable to find the poison in the hairs and pollen from these plants.

In this investigation we shall undertake to inquire into the histological nature of the stems and leaves of *Rhus venenata* and make observations on its poisonous constituent.

The specimens used in this work were collected near Atco, New Jersey, in July of 1919, and allowed to dry. The Martindale Herbarium of the Philadelphia College of Pharmacy and Science was consulted and proved of considerable value.

DESCRIPTION OF PLANT.

Rhus venenata De Candolle, family *Anacardiaceae*, is commonly known as swamp-sumac, poison sumac, poison elder and poison dogwood. The latter synonym must not be confused with the flowering dogwood, which is a member of the *Cornaceae* family.

It is a shrub possessing a slender clustered stem, which sometimes takes a tree-like form, reaching to a considerable height. The stem is brittle, showing for the most part a pithy region internally. The leaves are 7–13 foliate, with slender reddish green petioles. The leaflets are obovate, oblong, dark green and glossy on the ventral surface, paler on the dorsal side, and without marginal teeth. The midrib and veins are prominent. The flowers are diœcious and are in narrow axillary panicles, yellowish green to white in color. The petals are slightly reflexed. The stamens appear nearly twice as long as the petals. The fruit is a smooth, white drupe, often remaining on the branches until spring. The leaf scars are prominent, alternate and of a somewhat crescent shape. The bark on young stems is mottled with conspicuous lenticels.

HISTOLOGY OF STEM.

We find the epidermis to be composed of a single layer of epidermal cells with a thick outer cuticle. The subepidermal region shows a couple of layers of cork cells, more or less tangentially elongated. The cortex region is compact in nature and consists for the most part of sclerosed parenchyma. Numerous rosette, aggregate crystals of calcium oxalate are found in this region. Resin canals are present in the primary cortex, which, according to Solereder[4] is common in the *Rhus venenata*. The structure of the pericycle varies according to the age of the plant. In the older stems isolated groups of sclerenchyma fibers occur usually in the form of adjacent arcs. The convex side of each of these is directed towards the exterior. The inner concave side of each arches over a dome-shaped phloem in the centre of which is a single resin canal. In younger stems the arcs (strands) of sclerenchyma fibers are joined with each other by means of sclerosed parenchyma. In this way the pericycle constitutes a continuous ring of stereomatic structure, which covers the phloem-containing resin canals as a single band. A zone of cambium cells, more or less collapsed, is found separating the phloem region from the xylem. The prosenchyma forming the structure of the wood has simple and bordered pores. The

medullary-rays are usually one and two cells wide, with four cells as the maximum width. As stated by Solereder,[4] the resin canals, which are characteristic for the plants of the Anacardiaceae, often extend from the bast region and penetrate into the medullary region,

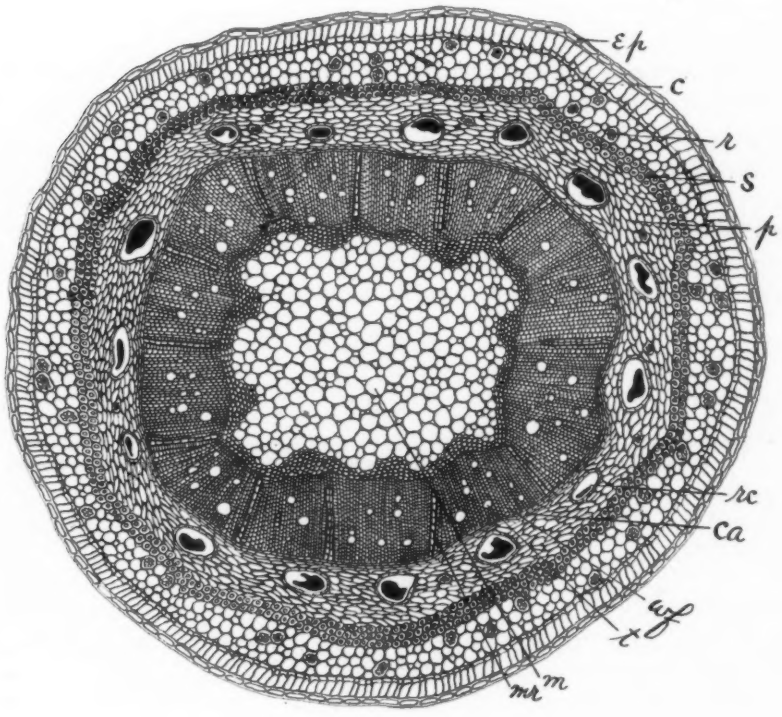

Fig. 1.—Transverse section of young stem of *Rhus venenata* DC. Epidermis (*ep*); cortex (*c*); rosette crystals of calcium oxalate (*r*); continuous ring of stereomatic tissue in pericycle (*s*); phloem (*p*); resin canals (*rc*); cambium (*ca*); xylem (*x*); wood fibers (*wf*); and tracheae (*t*) of the xylem; medullary rays (*mr*); pith (*m*).

where they end blindly. The canals are narrow-branching vessels filled with a dark reddish brown substance of a resinous nature. This substance responded to the cyanin test for resin. It did not react to the chemical tests for gummy lignin as noted by Youngken[5]

in stems of the *Myricaceae*. On treatment with alcoholic potash solution the resinous material combines with it to form a nigrescent compound. This reaction is characteristic[3] of the poisonous substance causing the dermatitis produced by poisonous species of *Rhus* plants. The pith consists of thin-walled parenchyma cells with an occasional duct.

HISTOLOGY OF LEAF.

The lamina is of dorsiventral structure. A layer of thin-walled cells forms the epidermis of the ventral surface. In the mesophyll region there is a ventral stratum of palisade tissue and a dorsal pneumatic tissue of large roundish cells, which often contain rosette crystals of calcium oxalate. Stomata lacking subsidiary cells and raised a little above the adjoining epidermis are present in the dorsal epidermal region. The resin canals, which were present in the fibrovascular bundles of the stem, also accompany the vascular bundles

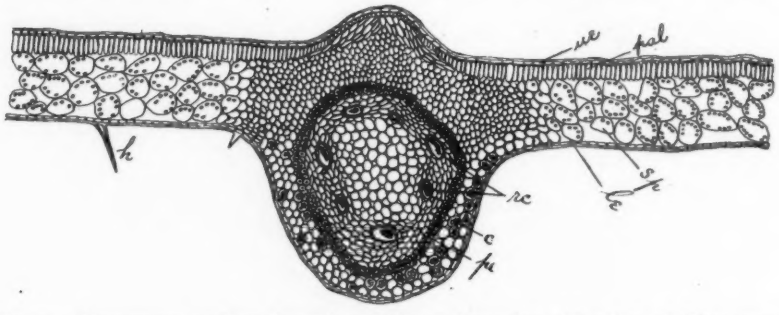

Fig. 2.—Transverse section through midrib and portion of lamina of *Rhus venenata*. Upper epidermis (*ue*); palisade parenchyma (*pal*); spongy parenchyma (*sp*); lower epidermis (*le*); resin canals (*rc*); rosette crystals of calcium oxalate (*c*); pericyclic fibers (*pe*); hairs (*h*).

of the leaf in both the larger and smaller veins. Collenchyma tissue is present in the dorsal region of the midrib. Non-glandular unicellular and uniserate hairs are found in the dorsal region. They are present in greater number along the veins. Many contain the "resinous substance" of Schwalbe, which responds to the nigrescent reaction when treated with alcoholic potash solution. Schwalbe[3] accounts for the presence of this resinous material in the hairs of *Rhus toxicodendron* as a product of osmosis from the neighboring lacticiferous vessels containing the resin. In the *Rhus venenata* resin canals are found to be the conducting vessels. As the resin

canals were not found to penetrate the mesophyll region, the presence of the resin in the hairs may be due to osmosis. We are inclined to believe it may be a direct product of the protoplasm, which the authors hope to report in a later article.

In the approximate chemical analysis the dried leaves and petiole were passed through a number 60-mesh sieve. This yielded a dark green-colored powder with a very peculiar, offensive odor.

The sample being in a dry state, oxidation and change of character of some constituents most likely took place, which must be considered.

On ignition the powder yielded 6.5% ash content. The residue was grayish brown and had an alkaline reaction. Traces of potas-

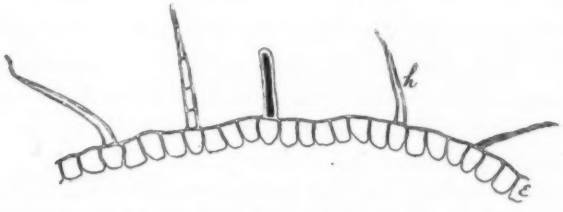

Fig. 3.—Vertical view of portion of dorsal epidermis of *R. venenata* lamina. Epidermal cells (*e*); non-glandular hairs (*h*).

sium, chlorides, phosphates and sulphates were found in the ash. Nitrogen was determined by the Kjeldahl method. The presence of nitrates and nitrites could not be found.

Four extractions were carried out by the Soxhlet continuous extraction method. Each extraction extended over a period of 3 days, allowing the solvent to macerate the sample during the nights.

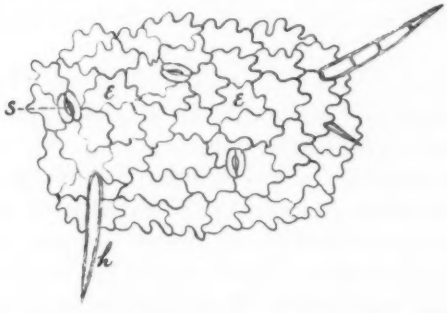

Fig. 4.—Surface view of dorsal epidermis of *R. venenata* lamina showing hairs (*h*); wavy walled epidermal cells (*e*); and stomata (*s*).

A good grade of low-boiling petroleum ether was used in the first extraction. In this solvent ethereal and non-volatile fixed oil was obtained, as well as a great amount of chlorophyll. On standing a white waxy-like substance separated out of the petroleum extract.

By spontaneous evaporation of a portion of the petroleum extract a yellowish brown, oily residue was obtained. This residue, when taken up with neutral alcohol, is neutral in reaction.

The alcoholic solution of the residue was optically inactive, which Pfaff states is true of the non-volatile oil causing the dermatitis.

The residue from the petroleum ether extract, when taken up with alcoholic potash solution, can be saponified. No glycerin is liberated.

To confirm, practically, that the poisonous principle was obtained in the petroleum ether extract, the same was applied to the inner forearm with a piece of cotton and allowed to remain. In twenty-four hours inflammation with violent itching occurred and in thirty hours vesication had taken place.

An alcoholic solution of the residue, when treated with a solution of lead acetate, will cause precipitation of the lead salt of the oil to take place. By treatment of this lead compound with hydrogen sulphide, Stevens was able to isolate the oil from the *Rhus toxicodendron*.

As irritation is often due to precipitation of proteins, experiments were made to precipitate egg and blood albumen from 0.5 per cent. solutions, by treatment with an alcoholic solution of the residue from the petroleum ether extract. Negative results were obtained. More extensive experimentation with oil obtained from fresh plants is hoped to be carried out in a continued article by the authors.

In the presence of fixed oil, alkaloids are often extracted simultaneously by petroleum ether, but no alkaloids could be extracted from the stems or leaves of this plant.

The second extraction was with ether. This was not carried out until all the petroleum ether had evaporated from the marc.

The ether extract was dark red-brown in color, which yielded a residue of the same color. When taken up with neutral alcohol the reaction was unchanged. Precipitation took place when the ether extract was treated with lead acetate solution. An alcoholic solution of the ether residue will precipitate a resin out of solution

when poured into water. No poisonous principle was found in the ether extract when applied to the inner forearm.

The alcoholic extraction which was carried out after all the ether evaporated yielded a yellowish brown solution in which tests for tannin were positive. No poisonous constituent was found in the alcohol extract.

The water extract gave tests for mucilaginous substances when mixed with alcohol by precipitating them out of solution. Fehling's solution was reduced by the aqueous extract.

At the present time no reliable form of treatment for the dermatitis caused by these plants is known. What will often effect relief in some cases will be obstinate and often assist perverse conditions to develop in other individuals.

That immunity may play a part is believed by some scientific workers, but this generalization is more common among the laity.

Cases of *Rhus* poisoning in the winter months are frequently met with, and are accounted for by the presence of the hairs on the stems and branches throughout the entire year.

Generally the hairs penetrate into the sudoriferous and sebaceous glands. This observation is corroborated by the fact that parts of the skin perspiring easily are affected most frequently by the poisonous principle.

Whether this non-volatile oil is taken up by the blood to form toxic substances is a field for biological research in connection with the comparative toxicity of the oil from *Rhus toxicodendron* and *Rhus venenata*, respectively.

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THE PHARMACOLOGICAL ACTION OF ADONIS VERNALIS.

By James M. Schmidt, M.D.

From the Biological Laboratory of the Upjohn Company.

Adonis Vernalis, or Pheasant's eye, is named among the drugs which possess the power of stimulating the heart. Its position in the group of digitaloid drugs is dependent upon a rather limited amount of experimental work, and a few instances of its clinical use. In the following we review the previous work upon the plant and add the results of our own investigation.

The literature with reference to *Adonis Vernalis* may be briefly reviewed as follows:

In 1882, Cervello[1] reported on the pharmacology of adonidin, the "glucosidal" active principle of adonis. This report consisted chiefly of the clinical results of its administration and a demonstration of its action upon the heart and blood pressure in mammals. His conclusion states that adonis is very similar to digitalis, in that it slows the heart, and increases the blood pressure in mammals; and that toxic doses will stop the frog's heart in strong systole with the auricles widely dilated, just as is the case in a digitalis heart.

Fucklemann[2] in 1911, reported on the chemistry and pharmacology of the drug, also giving the results in a few cases of its clinical application.

During 1913, Slovtzov[3] concluded that adonis regulates the action of the heart, slows its rate, and strengthens its beat; but that it increases the rate of the heart in cold blooded animals.

Chevalier[4] stated that adonis is like squills and not like digitalis, and that its principle effect is a stimulation of the kidneys. During the same year, 1913, Fucklemann[5] said that adonidin possessed digitaloid effects.

In the year 1914, Mercier[6] repeated Fucklemann's experiments and concluded that "adonidic acid" contained in adonis, had a paralysing and contracting action upon the heart muscle, and is very similar to the digitonin in digitalis. Also in 1914, Roch and Cramer[7] claimed that large doses of adonis were insufficient in cardiac diseases.

In 1918, Heyl, Hart and Schmidt[8] published the results of a thorough chemical examination of adonis leaves. They analyzed various extracts of adonis and compared with these the toxicity as determined by the one-hour frog assay.

In the following work an attempt has been made to compare

galenical adonis extracts with digitalis and the other cardiac stimulants, both as to strength and to action.

THE ACTION OF ADONIS UPON THE FROG'S HEART.

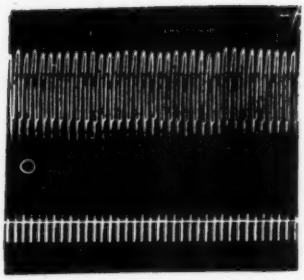
Frogs, of the type Rana Pipiens, which have received toxic doses of adonis, show but slight irritation. Their attitude is rather one of depression until shortly before their heart stops beating, when they show evidence of some discomfort. The ability to control voluntary movements, however, often remains after the heart has stopped, for having been injected with a toxic dose of adonis, the frog may hop about normally, and make every effort to avoid being caught; but after pithing and opening its thorax, it will have a heart which is stopped in permanent systole. This would tend to show that the drug acts more upon the heart than upon the central nervous system in general.

The following table is a typical chart of a frog's heart poisoned with adonis.

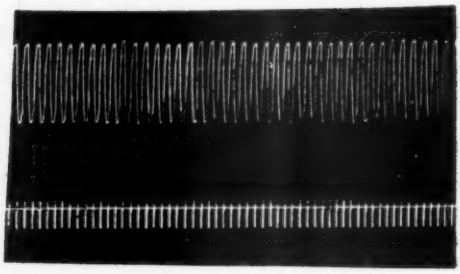
18 gm. frog, brain pithed and heart exposed.

Time.	Rate of beat per minute.	Remarks.
1:49	33	
1:51		2 cc. of adonis injected into the lymph sac of of the leg.
1:54	33	
1:55	31	
1:58	29	The ventricle is paler and contracts more strongly.
2:00	23	
2:03	22	Auricles and ventricles beating strongly and in unison.
2:05	20	This is the rate of both auricles and ventricles.
2:10	14	Ventricles have stopped, this is auricular rate.
2:12		Auricles are still beating, though irregularly, the ventricle is contracted firmly and does not beat.
2:15		The auricle has stopped beating and is widely dilated. The ventricle is small and pale in color.

Although the systolic effect of the drug is evident from careful examination during several autopsies, it is demonstrated in the tracings as 1-C, by the increased distance between the mark of the lever and the base line. In many instances there is some increase in

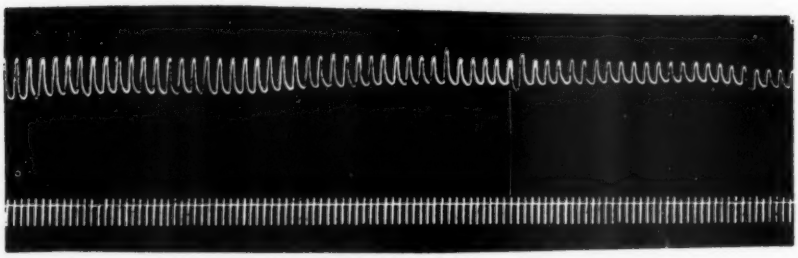


Tracing 1-A. From a normally beating frog's heart.



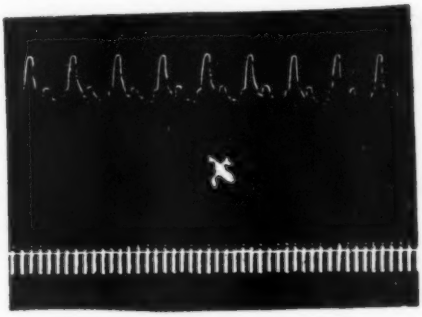
Tracing 1-B. From a frog's heart shortly after the application of adonis; showing a slightly slower rate of beat.

dilatation shown shortly after the application of the drug; this is always immediately followed by a lessened dilatation, as the lever rises higher and higher each succeeding diastole. Since the systolic contraction cannot raise the lever higher even by its increased



Tracing 1-C. The same tracing later.

strength, the excursions become gradually smaller until the heart finally stops. Records of the heart taken in this manner frequently show a one to two rhythm between the auricles and the ventricles in the latter stages of poisoning (see tracing 1-D); this indicates that adonis decreases the power of conduction between the auricles and the ventricles, in the same manner as does digitalis. The tracings 1-A, B, C, are very typical of the effect of adonis upon the heart's rate of beat. The heart is always slowed until it reaches the toxic stage when it becomes rapid and irregular. When the frogs heart has been stopped by adonis, it presents a very characteristic picture, namely, that the ventricular walls are firmly contracted so that they appear quite pale in color, the auricles being widely



Tracing 1-D. Showing the one to two rythms often displayed after the application of adonis. The time is marked in seconds, the lever moves upwards in systole and downwards in diastole.

dilated and filled with dark unoxygenated blood. In short the hearts appear to be typical digitalis hearts.

Since the frog hearts which had been poisoned with adonis, presented the typical digitalis picture, it seemed reasonable that adonis could be assayed by the one-hour frog method which is official for digitalis.

THE ASSAY OF ADONIS.

The information with regard to adonis has been derived from work done upon two lots of the drug, which we have called Drug A and Drug B. Alcoholic tinctures were made from these drugs at different times and they were assayed as follows:

DRUG A.

Per cent. of alcohol in the menstruum used.	Toxicity, or the minimum systolic dose (M. S. D.) per gram of frog.
95	0.0043 cc.
95	0.0043 cc.
80	0.0033 cc.
70	0.0033 cc.
60	0.0040 cc.
50	0.0027 cc.

This makes the average toxicity 0.0036 cc. per gram of frog.

DRUG B.

Per cent. of alcohol in the menstruum used.	Toxicity, or the M. S. D. per gram of frog.
95	0.0055 cc.
95	0.0045 cc.
50	0.00315 cc.
50	0.0043 cc.

The average toxicity of Drug B is 0.0043 cc.

From these results the average toxicity of Drug A is greater than that of Drug B. A total average for both drugs would be about 0.004 cc. of a tincture. In these assays the resistance of the frogs was taken into consideration; each lot was assayed against ouabain, as is ordinarily done in the assay of any of the heart tonics.

A tincture of adonis possessing a toxicity of 0.004 cc. per gm. of frog, was also assayed with guinea pigs, according to the manner followed in the twelve hour guinea pig assay of the heart tonics.[9] The pigs poisoned in this way, showed no peculiarly characteristic symptoms. They stand or lie quietly until near the very last, when they begin to struggle, and soon die. The assay is as follows:

Dose per Gm. of Pig.	Weight of Pig.	Actual Dose Given	Result in 12 Hours.
0.002 cc.	300 gms.	0.60 cc.	— living
0.003 cc.	340 "	1.02 cc.	— "
0.004 cc.	425 "	1.70 cc.	— "
0.005 cc.	330 "	1.65 cc.	— "
0.006 cc.	370 "	2.22 cc.	+ dead
0.007 cc.	415 "	2.905 cc.	+ "
0.008	425 "	3.40 cc.	+ "

Since we consider that a tincture of adonis, which assays 0.004 cc. by the one hour frog method is an average strength tincture; so we conclude that 0.006 cc. represents the average minimum lethal dose of adonis for guinea pigs.

THE IRRITATING PROPERTIES OF ADONIS.

Digitoxin, a comparatively insoluble constituent of digitalis, is extremely irritating to the mucous membranes. Adonis, on the other hand, is soluble and produces but little irritation. Upon the injection of digitalis into the lymph sac of a frog, a certain amount of hyperaemia of the abdominal epidermis is frequently noticed, even though the alcohol had previously been most carefully removed. This was never noticed in the numerous assays of adonis. Neither do

the frogs injected with adonis show the same amount of irritation as is so frequently seen in the digitalis frogs. They usually lie quietly until the very last, before showing any signs of discomfort.

One method of demonstrating the irritant properties of digitalis has been by perfusing frog hearts with physiological salt solution until they just stop beating.[10] Dilute digitalis preparations, either applied to the heart or introduced into the perfusing solution at this time, caused the heart to again start beating. Frog hearts treated in a similar manner with adonis, even with fairly strong solutions, could not be induced to again start beating. (Tracing 3-A and 3-B.)

Large doses of adonis administered orally to guinea pigs, rabbits and dogs, produced no vomiting and no apparent nausea, whereas the symptoms of digitalis poisoning are most constantly initiated by nausea and vomiting. As shown by Hatcher and Eggleston,[11] however, these symptoms may not be due to the irritation produced by the drug upon the gastric mucous membrane. They demonstrated that the intravenous injection of relatively small doses of digitalis to cats would produce emesis, even more readily than if administered orally, and that this action was probably due to its effect upon the central nervous system, rather than to any irritant properties that it might have upon the mucous membranes. They were able to produce emesis in dogs upon the intravenous injection of 0.5 mg. of digitoxin per kilo, while adonis required 65 mg. per kilo, or one hundred and thirty times as large a dose to produce the same result.[12] Whether the comparative lack of emetic properties possessed by adonis is due to the fact that it is non-irritating to the mucous membranes, or that it is unable to produce emesis by acting upon the medulla, the mere fact that it does not have the same amount of emetic action as digitalis might be a valuable therapeutic factor, for patients suffering from cardiac decompensation may suffer severely from gastric symptoms, and the administration of the emetic digitalis becomes most difficult.

THE ACTION OF ADONIS IN MAMMALS.

The blood pressure tracing shows three typical effects as taken from rabbits, following the intravenous injection of about one-half cc. of an average strength tincture of adonis. (Tracing 2.) There is an immediate rise in pressure, lasting on the average about five or ten seconds. After falling back to normal, there immediately

Tracing 2. This shows a typical blood pressure tracing as obtained from the insertion of a cannula into the carotid artery of a rabbit. In the course of one to two minutes the pressure returns to normal unless more adonis is given, in which case the heart passes into a typical toxic condition.

follows a more pronounced and more prolonged rise. In addition to this feature there is a marked slowing of the heart's rate, and frequently a clearly demonstrable increase in the pulse pressure. This increase occurs only in case there is a slowing of the heart's rate, and is the expected result upon the blood pressure of a strongly beating heart which is being slowed in rate, thus allowing the pressure to fall further between beats.

The effect of adonis upon the frog's heart has been previously discussed. Tracings 1-A, B, C, and D are typical of those produced by frog hearts whose action has been influenced by adonis. The hearts are markedly slowed in rate, show a decreased conduction between the auricles and the ventricles, and present an increase in the strength of the systolic contraction.

The reaction of the mammalian heart to adonis was studied in rabbits and dogs by means of the blood pressure tracings, and those obtained by the myocardiograph. The blood pressure record was taken from the carotid artery of rabbits, and shows a slowing of the rate of beat until a large amount of drug has been introduced into the blood stream, when the heart becomes irregular, many of its beats become inefficient, and there are large oscillations in the blood pressure resulting, until it finally falls as the heart stops beating. This heart, however, upon examination, is found widely dilated and in a diastolic condition.

In dogs, a myocardiographic record was made. This demonstrated that the rate of beat was slowed as in the other experiments, both auricles and ventricles showing this effect previous to the injection of sufficient adonis to produce an irregular or toxic action upon the heart. The increased systolic contraction becomes most evident here, being especially prominent in the ventricles. There is at times an increased dilatation, especially if the effect of the vagus nerve is not removed by atropine. Section of the vagi frequently has but slight effect, this factor however, being somewhat variable. Apparently adonis tends to a more peripheral stimulation of the vagus nerve than does digitalis; since in the experiments in which section of the vagi caused little change in the effects of adonis, there was a noticeable difference if atropine was administered. This consisted in less dilatation of the heart, instead of the increased dilatation usually produced by adonis; and also in a more rapid rate of beat instead of the slowed rate. This difference was not noticed when the same experiments were done with digitalis.

heart passes into a typical toxic condition.

Tracing 3-A.

Tracing 3-B. These tracings were made in the usual manner, but the hearts were perfused with Ringer's solution for frogs until they stopped beating. At X a few drops of digitalis were placed upon the heart. At O it was washed with Ringer's solution. At < adonis was applied.

It has been noted that digitalis has two distinct actions upon the mammalian heart. The one is a slowing of its rate, produced by relatively small doses of digitalis, and removed by section of the vagus nerves or by the administration of atropine. Adonis in a like manner, in small doses, produces a slowing of the heart's rate, which in all cases can be removed by atropine. This action may be termed the beginning of the action of digitalis, or of adonis, and is purely a slowing of rate. Another phase of digitalis action is shown however, in cases of the administration of large doses of digitalis, especially in cases of fatal poisoning. This is evidenced by a more rapid rate of beat, and persists even after section of the vagi, or the injection of atropine. Cushny.[10] If the adonis action were to be compared with digitalis, it was considered necessary to compare this action also. Large doses of adonis given after removal of vagus control, show an increased rate of beat.

In order to determine the action of adonis upon the relative lengths of systole and diastole, tracings were taken from rapidly revolving drums and compared with the record of a tuning fork which vibrated at the rate of one hundred times per second. In this experiment frogs were used, and adonis applied to the exposed tissues immediately surrounding the heart. The following are the results taken from a single heart, but are typical of each experiment performed.

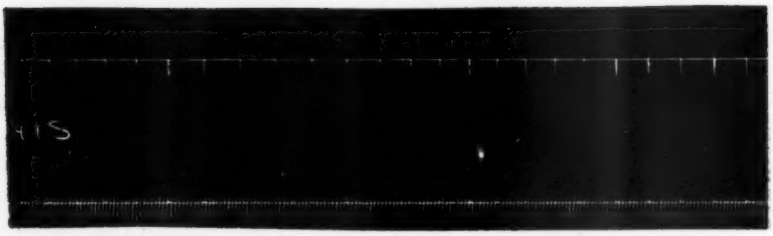
Measurements taken from the record made by the heart before adonis was applied gave the following results.

	Duration of Systole in One Hundredth of a Second.	Duration of Diastole in One Hundredth of a Second.
Readings.	70	38
	72	38
	69	38
Average.	70	38
Measurements Taken One Minute after the Application of Adonis.		
	82	55
	85	55
	82	50
		49
Average.	83	52
Measurements Taken Five Minutes after the Application of Adonis.		
	71	64
	75	60
	76	
Average.	74	62

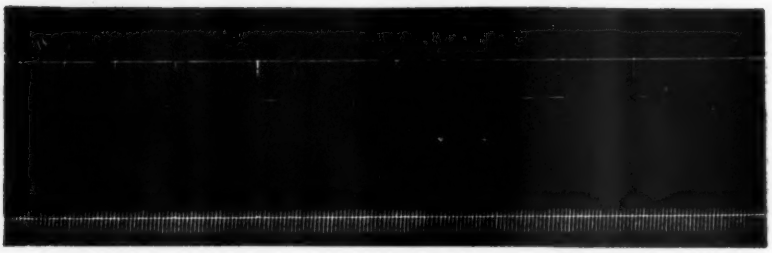
This shows an increase in the duration of both systole and diastole at first; the diastole being greatly increased in the later stages, while the systole is not quite so prolonged.

The effect of adonis on the peripheral blood vessels was determined by perfusing dilute solutions through the peripheral circulations of

Tracing 4-A.



Tracing 4-B.



Tracing 4-C.

Tracing 4-A. Shows the increased outflow from the venous cannula immediately following the administration of 0.3 cc. of adonis at arrow.

Tracing 4-B. A direct continuation of A, and shows a gradual slowing of the venous outflow, which becomes more marked in C.

frogs and rabbits. (Tracing 4.) In frogs a cannula was placed in the abdominal aorta and the drops recorded as they came from the median abdominal vein. A similar method was used in rabbits. The results in the two cases showed no variation. Ringer's solution was first perfused through, and after a normal or steady rate was ob-

tained, about a half mil. of alcohol-free adonis was introduced into the perfusing stream without producing an increase in pressure, and the effect recorded upon a drum, by means of an electrical drop recorder. As the result of this, there is shown at first a slight but very evident slowing of outflow. This is quickly followed by a more rapid output, and then as the drug continues to act, the drops come out more and more slowly. This demonstrates a temporary dilatation of the blood vessels, which at first will cause a slowing of the outflow, but as the perfusing solution continues to flow through the dilated vessels, the outflow is quickly increased. If larger amounts of adonis are placed in the perfusing solution, this first dilatation cannot be demonstrated, and even though small amounts of a dilute adonis are used, this preliminary dilatation is soon followed by a gradual and prolonged constriction of the vessels, so that the output of the perfusing solution from the vein is greatly decreased.

Experiments were carried out in exactly the same manner using digitalis, strophanthus, and squills. These drugs all produced the same effects in character, though strophanthus very evidently produces less effect upon the peripheral blood vessels than do digitalis or squills, and adonis gives results much more closely simulating digitalis than strophanthus.

It is to be noticed that the result of the effect of adonis on the blood vessels is most strictly comparable to the blood pressure tracings. The initial fall in pressure may be attributed to a temporary vaso-dilation, and the prolonged rise in pressure to a vaso-constriction. R. Joseph[12], gave small doses of the digitalis drugs and demonstrated that if they had an effect on the heart, that they also had an effect on the blood vessels. This statement seems somewhat doubtful, in view of the fact that we are able to produce a marked slowing of the heart rate without producing any change in the blood pressure. He does, however, find that the action of digitalis upon the blood vessels produces a dilatation as well as a constriction. He shows a dilatation occurring soon after the drug enters the blood stream, and lasting but a short time; while the constriction is more prominent and is more prolonged.

An attempt was made to determine the effect of adonis upon the kidneys. A cannula was placed in the ureters of a rabbit, and by means of a drop recorder a record of the urine outflow was obtained along with that of the blood pressure. While there was usually a demonstrable increase in the output of urine during the period following the action of adonis, still this action did not seem to present

the same degree of prominence which was present in the experiments in which digitalis was used.

CONCLUSIONS.

We conclude that *Adonis Vernalis* stimulates the heart in a manner very similar to digitalis; that it produces variations in blood pressure characterized by a rise, if large doses are administered, or by no pressure effect if the doses are relatively small; that the changes in pressure are caused mainly by the action of the drug upon the blood vessels; that it is less irritating than digitalis and possesses less tendency to produce a gastric disturbance; and that it possesses approximately the same strength as digitalis preparations made according to the official directions for a tincture or a fluidextract.

I wish to express my indebtedness to Dr. F. W. Heyl for many helpful suggestions during the preparation of this paper.

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INSECTS USED IN MEDICINE.

By John T. Lloyd, Ph.D.,

Cincinnati, Ohio.

That insects and their by-products play an important part in the economy of man is known to every layman. All appreciate the uses made of honey by civilized peoples and many know the still greater importance it holds in the diet of the savage who is unable to concentrate the dilute juices of plants to syrup or sugar. Many savage peoples also relish the fat larvae of certain insects, and thus the insects themselves play their part by breaking the

monotony of a scanty primitive diet. In the arts we all know that certain products of insects are of great importance—every household uses beeswax, every painter uses shellac—both are produced by insects. Perhaps however it is not so well known to the layman as to the physician that a few insects play an important rôle in the modern practice of medicine.

Chief among insects of medicinal value may be mentioned *Apis* (the honey bee) and *Cantharis* (a blister beetle). These almost alone from a host of insect preparations of ancient times retain their place in modern practice.

That a multitude of insects found their way into the practice of medicine during the medieval age seems to have been due not to their tried and proven therapeutic value, but to the fact that the people of the time were devoutly religious. They believed that the earth and all upon the earth were created to serve the interests of Man. Following this line of argument it was an easy matter for them to account for the Creator's purpose in making such important foods as wheat, fruit and vegetables but it sometimes became exceedingly difficult to find an ample reason for the creation of some of the lower forms of life. One has but to read some of the old volumes to realize to what absurd extremes men were driven to explain the Creator's wisdom in giving to Man some of the insects. For example according to the old authors, ants were made to set an example of industry to Man and lice were good because they kept him from sleeping too much and becoming lazy. Nevertheless, after taxing their ingenuity to the utmost, they seemed to be unable to find the reason for the creation of many insects. These they assigned to medicine, and it is likely that because they were thus assigned to medicine their therapeutic values were learned. If anyone doubts that small quantities of a certain insect can have a definite physiological reaction on the human body he has but to take the prescribed dose of Apis to be convinced, or if this be not, at hand let him try the sting of a bee.

That more insect remedies are not now used in the practice of medicine is due, possibly, rather to the objectionable form in which they were administered in the old prescriptions, than to the lack of value of the material. For example, what modern physician's patients would submit to swallowing a "spider wrapped in dough," or the "oil of angle-worms macerated a week in the sun?" If plant products, such as alkaloids and resins, have therapeutic value, why

should not some of the products of insects be likewise active? Not alone do the bodies of insects contain the ordinary products of animal metabolism, but many species have highly specialized glands peculiar to themselves, that manufacture and secrete complex chemical products. These, by some species, are used to attract the mate, by others to repel enemies, either by repugnance or as mechanical barriers. Everyone is familiar with the disagreeable odor of the "stink bug," and with the more pleasant odor of the bumble-bee—each peculiar to the species—and everyone who has handled great numbers of living insects must have noticed the large number of specialized secretions, in some species pleasant, in others disagreeable. Some secretions are oil-like liquids that cling to the insects, others are volatile vapors thrown into the faces of approaching enemies, others are waxes, or froth-like secretions. In all they are as distinct as are the products of plants, but the physiological reactions of nearly all of them are as yet untried.

This is but a general view of a subject that permits of most interesting detail extensions.

URINARY CASTS.*

By Louis Gershenfeld, Ph.M.

Urinary casts are, in most cases, derived from the renal tubes but occasionally casts obtained from the glands connected with the urinary tract, are met with. There are cases on record where casts of the larger urinary passages, most frequently of the ureter or urethra, have been found. These are not microscopic, but can be seen with the naked eye, measuring in some instances as long as 3 or 4 inches. The latter are usually derived from cases associated with tumors of the bladder or kidney. Renal casts are almost invariably associated with albumin, present or recently present in the urine; and, with few exceptions, they indicate some pathological change in the kidney. After severe exertion, however, or during some temporary irritation or congestion, they may be found in the urine. They remain intact for a considerable length of time in acid urine, but quickly lose their shape and disappear in alkaline urines. It is for this reason that the search for casts must be made carefully from a fresh sample, for urine, upon standing, frequently becomes alkaline in reaction.

* Read at the annual meeting of the Pennsylvania Pharmaceutical Association, Harrisburg, June, 1920.

The diameter of the different types of casts show a characteristic uniformity. The sides are usually parallel, while at the two extremities one is either pointed or rounded, and the other is frequently broken across. The structure may otherwise be straight or convoluted, while the length varies considerably.

Though it is difficult at times to distinguish between the different varieties, casts have been classified, according to their microscopical characteristics as follows: hyaline casts; waxy or colloid casts; granular casts (fine and coarse); epithelial casts; fatty casts; blood casts; pigment casts; leukocyte, pus or purulent casts; fibrinous casts; bacterial casts; calcareous casts; ammonium urate casts; spermatic casts.

The source of the albuminous material, making up the composition of a cast, is not known. Some claim that they are the products from broken down epithelial cells, contrary to the belief of others, who think that they are abnormal secretions thrown off by diseased renal cells. Other investigators have formed the opinion that the blood plays an as yet unknown rôle in the production of these pathological substances.

Though their source is still in doubt, it is, however, the belief of most workers, that this albuminous product enters the uriniferous tubules in such a physical state, as to be capable of being easily molded. It is also held that they are formed in the straight tubules, and not in the convoluted tubes. The casts assume the shape of the tubule, retaining within their structure whatever substances were lying free, and then bend themselves up, or are forced to assume a wavy or convoluted shape, due to the obstacles they meet as they are forced out by the pressure of the urine. It is for this reason that the various forms are met with. There apparently seems to be no definite relationship between the number of casts present and the severity of a morbid process.

Hyaline Casts.—These are the most frequently observed casts, found in almost all kidney disorders, and occasionally in transitory conditions. They are straight or convoluted, transparent, homogeneous, and very delicate in structure. Their length and breadth vary, while their form may show marked variations. These casts are frequently coated more or less completely with albuminous débris or other granular material, such deposits giving a granular appearance to the casts. The impregnations commonly observed are various cells, either epithelium, erythrocytes, leukocytes or the

products of their disintegration, or non-organized constituents, as urates. Hyaline casts differ from cylindroids, which they so closely resemble:

1st. Tube casts do not form sharp angular bends, as found in cylindroids.

2nd. Cylindroids always exhibit a longitudinal striation, and are usually considerably longer.

3rd. Cylindroids do and hyaline casts do not give the mucin reaction (the production of coarsely granular turbidity (observed microscopically) on the addition of acetic acid).

Waxy (or Colloid) Casts.—The term waxy has been one of considerable misunderstanding and confusion. Colloid is a better term to use. The term waxy should only be used for those casts that possess a lardaceous or waxy composition. They give no precipitate with acetic acid, nor do they swell under the action of this acid. Their composition possesses all the characteristics of that widely discussed, ill-defined and yet unknown material, called by the name of colloid substance. It is thought that these casts are formed by an alteration of albuminoid material, produced by degeneration of renal epithelial cells. This accumulating in the tubules, probably gets mixed with other exudations from the blood vessels, and what is known as colloid casts result. It is on this account that these casts are found most frequently, associated with chronic renal diseases, and are usually indicative of serious lesions.

Colloid casts have a peculiar, dull, opaque appearance (being more opaque than the hyaline casts), always broader than the latter variety, frequently shorter, but may vary considerably in length, and are either longitudinally fissured and with more or less irregular broken ends. The boarders are sharply defined and show indentations. Colloid casts of large diameter and length if present, can only be observed, providing great care is used in the treatment of the urinary sediment. At times they may possess a light yellow color. They are generally straight, rarely convoluted, and granular deposits are not frequently found in them.

Granular Casts.—Many regard these casts merely as hyaline material in which are embedded numerous granules. From the standpoint of accuracy, this is a mistake, as there is a difference between a granulated hyaline cast and a granular cast. The latter are short thick bodies, possessing a somewhat dark appearance and granules throughout. These granules consist of albumin (in rare

instances fat), and may be fine or coarse, giving rise to finely granular and coarsely granular casts. The granulated hyaline casts are longer, narrower and lighter. The granules are not as coarse and irregular transparent areas are apparent. These granules are composed of amorphous urinary salts (usually urates), which dissolve upon the addition of a drop of acetic acid.

Epithelial Casts.—Epithelial casts consist mainly of the epithelial cells lining the uriniferous tubules, and these casts are at times found covered with mineral and organic deposits. The individual cells are of varied shape and size, with a usually distinct nucleus. Epithelial casts are observed frequently in acute pathological conditions of the kidney.

Fatty Casts.—Under this heading are included casts in which the greater part of their surface area is covered with fat globules or crystals of fatty acids. They are met with usually in fatty degeneration of the kidneys.

Blood Casts.—Casts densely covered with erythrocytes constitute what is known as blood casts. The individual red blood cells may be of normal appearance, but more frequently they are decolorized and swollen. Occasionally other abnormal shapes are observed, representing various stages of degeneration. They are usually indicative of the occurrence of hemorrhage, which is not uncommon in acute renal disorders.

Pigment Casts.—In the later stage of renal hemorrhage, the blood cells in the cast are usually disintegrated. The breaking down of the erythrocytes leaves only flakes of pigment, which become imbedded within the cast, and form what is known as pigment casts.

Leukocyte, Pus or Purulent Casts.—In a chronic suppurative renal condition, which is not so frequently observed, these casts are met with. They are usually hyaline casts, thickly coated with masses of leukocytes, which may be of normal shape and size, or in a degenerative state. At times, they are mistaken for epithelial casts. Upon the addition of acetic acid, the neuclei become visible and the differentiation between these two types becomes easy.

Fibrinous Casts.—In cases of renal hemorrhage, there may be found casts composed almost entirely of coagulated fibrin. Upon the addition of acetic acid, they become almost invisible.

Bacterial Casts.—These are rare. They may be occasionally found in cases of suppurative nephritis. They differ from the true

casts, which are only occasionally covered with bacteria. These casts consist entirely of bacteria, usually the pyogenic cocci, closely packed together. They are differentiated from any granular debris, by their uniform shape and size, and also due to the fact that they are easily stained with aniline dyes.

Calcareous Casts.—There are few cases on record where true casts, exact moulds of the renal tubules, were observed in the urine of adults suffering with diseases leading to the formation of renal calculi. These were found to be either the phosphate or carbonate of calcium.

Ammonium Urate Casts.—Casts giving the reactions of ammonium urate have been met with in the urine of the new-born and other infants. According to many observers, their presence seems to have very little significance as a distinguishing feature in diseases.

Spermatic Casts.—These have been reported by some in cases of spermattorhea. They are said to closely resemble hyaline casts, except that they are, as a rule, much longer and broader. The apparent absence of albumin is an important fact for differential diagnosis. No one has as yet established clearly the origin of these casts.

Pseudo Casts are bodies, of varied inorganic or organic origin, possessing somewhat a resemblance to true urinary casts, and may be mistaken at times by the inexperienced for true casts. Unlike the latter, these false casts have no definite relationship to renal disorders. Masses of urates, phosphates, oxalates, uric acid and other crystals, deposited on shreds of mucus, or crystallizing on other filamentous structures, produce forms, distantly resembling casts. The use of heat and appropriate microchemical reagents and practice will soon allow the inexperienced to avoid these as a source of error.

A NEW METHOD FOR THE ESTIMATION OF METHYL ALCOHOL.*

By S. B. Schryver and Cyril Christian Wood.

A. Estimation of Methyl Alcohol in Water.—Some years ago, one of the authors described a method for the detection of formaldehyde, which could be applied to the quantitative estimation of very small amounts of this substance (*Proc. Roy. Soc.*, 1910, B. 82: 226,

*From *The Analyst*, May, 1920.

and Reports of Inspector of Foods, Local Government Board, 1909, N. S. No. 12; also *Analyst*, 34: 470, 1909). The method in question consisted in treating the solution containing the formaldehyde with 1 per cent. solution of phenylhydrazine hydrochloride, then adding potassium ferricyanide, and afterwards concentrated hydrochloric acid, when, in the presence of the aldehyde, a brilliant fuchsine-like color was produced, which could be detected even when the concentration of formaldehyde did not exceed 1 in 2,000,000. This reaction forms the basis of the method for estimating methyl alcohol described in the present communication.

Several reagents are capable of oxidizing methyl alcohol to formaldehyde, but most of these interfere with the application of the test described above. This was not found, however, to be the case when ammonium persulphate was used. If an excess of the persulphate is added, the formaldehyde is oxidized further to carbon dioxide and water. By ascertaining the amount of persulphate that must be added to a given solution of methyl alcohol in water, so that after completion of the reactions under certain standard conditions of experiment formaldehyde just fails to be detectable by the above-mentioned reaction, the percentage of the alcohol present in the water can be estimated with a considerable degree of accuracy, even when the amounts present are as low as 0.0005 per cent.

When ammonium persulphate is heated with a solution of methyl alcohol three reactions can take place simultaneously, *viz.*, the decomposition of the persulphate itself, the oxidation of methyl alcohol to formaldehyde, and the oxidation of the aldehyde. It is, therefore, necessary to specify accurately the conditions under which the estimation should be carried out, as is the case in other oxidation methods, such as that of Fehling's, where several oxidation processes take place at the same time.

The method of carrying out the estimation is as follows: Samples, each of 5 Cc. of the methyl alcohol solution in water are introduced into a series of test-tubes (6 inches by $^3/_4$ inch), and mixed with 5 Cc. of ammonium persulphate solution of varying concentrations. The test-tubes containing these mixtures are then inserted into a water bath containing boiling water, in which they are kept immersed for 10 minutes. At the end of this period 1 Cc. of the mixture is pipetted out from each tube and introduced into a series of smaller test-tubes, each of which contains 1 Cc. of 1 per cent. solution of phenyl-hy-

drazine hydrochloride; to these mixtures are then added 1 Cc. of a 2.5 per cent. solution of potassium ferricyanide and about 3 Cc. of concentrated hydrochloric acid. It will be found from this preliminary series of experiments that the concentration of methyl alcohol will lie between two limits—*viz.*, a higher limit corresponding to a concentration of the persulphate which is sufficient to oxidize completely the formaldehyde formed in the reaction, and a lower limit in which the concentration is insufficient, and the mixture of persulphate and methyl alcohol solution still gives a positive reaction for formaldehyde after heating for ten minutes. A second series of experiments can then be carried out in a similar manner to the first, mixing 5 Cc. of the methyl alcohol solution with 5 Cc. of persulphate in concentrations varying only between the two above-mentioned limits. The number of mixtures in this series can be varied according to the degree of accuracy which is desired in the estimations. If, for example, it was found that the mixture of 5 Cc. methyl alcohol solution mixed with 5 Cc. of 4 per cent. persulphate gave a negative reaction for formaldehyde in the first series of experiments, while the solution mixed with 5 Cc. of a 3 per cent. solution gave a positive reaction, in the second series of experiments the methyl alcohol solution was mixed with ammonium persulphate solutions varying only between 3 and 4 per cent. For each concentration of methyl alcohol, therefore, there corresponds a definite concentration of this persulphate which is just sufficient, under the specified conditions of experiment, to oxidize all the formaldehyde which is formed in the reaction.

TABLE I.

Per Cent. Persulphate in 5 Cc. Used for Oxidation.	Per Cent. of Solution of MeOH Used.	Cc. of This Solution in 10 Cc. Mixture.	Formaldehyde Reaction.	Concentration of MeOH in 5 Cc. Aqueous Solution.
5.0	1.0	1.45	+	0.29
5.0	1.0	1.40	0	0.28
4.0	0.5	2.4	+	0.24
4.0	0.5	2.3	0	0.23
3.0	0.25	3.45	+	0.1725
3.0	0.25	3.40	0	0.170
2.0	0.25	2.3	+	0.115
2.0	0.25	2.25	0	0.1125
1.0	0.1	2.8	+	0.056
1.0	0.1	2.7	0	0.054
0.5	0.1	1.5	+	0.030
0.5	0.1	1.4	0	0.028

0.25	0.05	1.5	+	0.015
0.25	0.05	1.4	0	0.014
0.10	0.025	1.0	+	0.0050
0.10	0.025	0.9	0	0.0045
0.05	0.010	1.3	+	0.0026
0.05	0.010	1.2	0	0.0024
0.025	0.005	1.3	+	0.0013
0.025	0.005	1.2	0	0.0012
0.010	0.001	2.5	+	0.00050
0.010	0.001	2.4	0	0.00048

In the above table are given the concentrations of methyl alcohol which are completely oxidized (so as to give a negative formaldehyde reaction) by concentrations of persulphate varying from 0.001 to 5 per cent.

The above table represents the final results of a detailed series of experiments, of which one is given *in extenso* to illustrate more clearly the method employed.

To determine the concentration of the solution of methyl alcohol which is just oxidized by a 5 per cent. persulphate solution, so that no formaldehyde is present after heating the mixture for ten minutes:

First Series:		Reaction (Formaldehyde).
5 Cc. of this 5 per cent. persulphate solution +		
5 Cc. of 1 per cent. solution of methyl alcohol	.....	strong pink
4 Cc. of 1 per cent. solution of methyl alcohol	1 Cc. H_2O	pink
3 Cc. of 1 per cent. solution of methyl alcohol	2 Cc. H_2O	pink
2 Cc. of 1 per cent. solution of methyl alcohol	3 Cc. H_2O	pink
1 Cc. of 1 per cent. solution of methyl alcohol	4 Cc. H_2O	0

Hence the concentration of methyl alcohol solution, 5 Cc. of which is completely oxidized by 5 per cent. persulphate, lies between $^1/_5$ and $^2/_5$ of one per cent.

To determine the concentration more accurately, the following second series of experiments was carried out:

		Reaction (Formaldehyde).
5 Cc. persulphate solution +		
1.5 Cc. of 1 per cent. solution of methyl alcohol	3.5 Cc. H_2O	faint pink
1.45 Cc. of 1 per cent. solution of methyl alcohol	3.55 Cc. H_2O	just pink
1.4 Cc. of 1 per cent. solution of methyl alcohol	3.6 Cc. H_2O	0
1.3 Cc. of 1 per cent. solution of methyl alcohol	3.7 Cc. H_2O	0
1.2 Cc. of 1 per cent. solution of methyl alcohol	3.8 Cc. H_2O	0
1.1 Cc. of 1 per cent. solution of methyl alcohol	3.9 Cc. H_2O	0

Thus, if the end-point is taken to be that concentration which just gives the pink formaldehyde reaction after heating for ten minutes with the persulphate solution, it will be found that 5 per cent. of the latter just oxidizes 5 Cc. of a solution containing $\frac{1.45}{5} \times 1$ per cent. = 0.29 per cent. methyl alcohol. The percentages of methyl alcohol corresponding to the various concentrations of persulphate are given in the final column of Table I. It is obvious that the concentration of a persulphate solution just necessary to oxidize a given concentration of methyl alcohol is a linear function of that concentration, and if c be the concentration (per cent.) of the persulphate, x that of the methyl alcohol, and k a constant, then $x = kc$. If this be calculated from the above table (neglecting the data for percentages of persulphate below 0.25 per cent.) k will be found to be = 0.059. These data were obtained with a methyl alcohol sample which had the correct boiling point, after careful fractionation over lime, and with a sample of persulphate in which the amount of ammonium persulphate was estimated by warming with a definite amount of standardized ferrous sulphate solution and determining the amount of the latter oxidized by titration against permanganate solution; this sample was found to contain 98.6 per cent. ammonium persulphate. In a series of experiments carried out with another sample of persulphate which was less pure, the constant k was found to be 0.054. In carrying out the estimation of methyl alcohol by the method above described, with any given sample of persulphate it is best to standardize 5, 4 or 3 per cent. solutions against methyl alcohol and to determine directly the constant k. Only a few experiments will be necessary, as the results will only differ slightly (by fractions of a Cc.) from the numbers given in Table I, column 3.

B. Estimation of Methyl Alcohol in Ethyl Alcohol.—An attempt was made to estimate methyl alcohol in ethyl alcohol by the same method as that employed for estimating the methyl alcohol in water. This was found, however, to be impracticable, and there is no preferential oxidation of the lower alcohol by persulphate. It was found, for example, that the amounts of the latter necessary to oxidize to the end-point (disappearance of formaldehyde) did not differ, outside the limits of experimental error, with ethyl alcohol mixtures containing 4 and 5 per cent. of methyl alcohol. Another

method had therefore to be employed. This consisted in treating a persulphate solution with an excess of the mixture of alcohols, and examining the products produced in the initial stage of oxidation. It was then found that, under conditions such as these, the larger the amount of methyl alcohol present, the greater the amount of formaldehyde present, when the limited amount of persulphate used was entirely decomposed. The amount of formaldehyde produced under the conditions of the experiment could then be estimated colorimetrically. The estimations were carried out as follows: Ten Cc. of the ethyl alcohol containing methyl alcohol are diluted with 50 Cc. of water. Five Cc. of this are then mixed with 5 Cc. of a 1 per cent. solution of ammonium persulphate in a test-tube; this is provided with a short air condenser and heated in a boiling water bath for ten minutes. At the end of this period, 1 Cc. of the mixture is added to 1 Cc. of a 1 per cent. solution of phenyl hydrazine hydrochloride, *with which it is heated in a boiling water bath for five minutes*. After cooling, 1 Cc. of a 2.5 per cent. solution of potassium ferricyanide is added, and then 3 Cc. of concentrated hydrochloric acid. A pink color is thereby produced when methyl alcohol is present, which can be compared with the colors produced in a similar way from samples of ethyl alcohol containing known amounts of methyl alcohol. Experiments have been carried out with mixtures of ethyl alcohol and methyl alcohol, when the latter varied from 0.5 to 5 per cent., and it is possible by this rough comparison to estimate the percentage of methyl alcohol when contained within these limits to within 1 per cent. A more accurate estimation can be obtained when a colorimeter is employed. The method of carrying out the more accurate determination is described below.

It will be noticed, in the directions given above, that the reaction mixture is *heated* with the solution of phenylhydrazine hydrochloride before the other reagents are added, when carrying out the test for formaldehyde. The reason of this is that during the reaction certain quantities of the ethylal $HCH(OC_2H_5)_2$, and probably of the methylal $HCH(OCH_3)_2$, are formed during the heating, and the full pink color is not given by formaldehyde combined in these ways, unless the mixture is heated with the solution of phenyl hydrazine hydrochloride before adding the other reagents. (Compare Schryver, *Loc. cit.*)

In carrying out the more accurate colorimetric estimations, the pink test solutions prepared by the method described above were diluted with 70 Cc. of water, and the color was then compared with a

standard prepared in an exactly similar way from a sample of ethyl alcohol containing a known amount of methyl alcohol. When a colorimeter of Schmidt and Haensch was used, differences could be detected between samples of ethyl-methyl alcohol mixtures in which the amounts of methyl alcohol differed by only 0.2 per cent. Possibly, with a more modern form of colorimeter, more accurate estimations would be possible. The researches on the determination of the amounts of methyl alcohol in ethyl alcohol have, up to the present, been confined to mixtures containing between 0.5 and 5 per cent. of the former.

The sample of ethyl alcohol gave a faint formaldehyde reaction when oxidized, and the oxidation products were tested for methyl alcohol in the manner described above. Whether this is due to the fact that it contains small amounts of the lower alcohol, or to the fact that formaldehyde is formed in small amounts by the oxidation of ethyl alcohol, it is impossible at the present to say.

C. Estimation of Methyl Alcohol in Acetone.—It was found that a similar method could be applied to the estimation of methyl alcohol in acetone to that employed for estimating this alcohol in water, as the acetone is only oxidized to a slight extent by persulphate. In the former case, however, there were certain difficulties in carrying out the estimation, which have necessitated, when the percentage of methyl alcohol present is small, certain minor modifications in the process. It was found when the acetone contained 4 per cent. or more of methyl alcohol that, as a certain concentration of persulphate was exceeded, there was a sudden transition from the bright pink color yielded by the formaldehyde test to a light pink, and this latter color persisted even when the above-mentioned concentration of persulphate was considerably above this transition point. This phenomenon is probably due to the formation of a condensation product of formaldehyde with acetone, which is very resistant to oxidation by persulphate. When the amount of methyl alcohol in acetone falls below 4 per cent., the transition point is not very marked. At 4 per cent. and over, when higher concentrations of persulphate must be used, the point is unmistakable; for each given concentration of methyl alcohol in acetone, under the conditions of experiment described below, there corresponds a given concentration of persulphate, a small addition to which causes a sudden transition from a bright pink to a light pink, when the formaldehyde test is applied. By this method it is easy to determine

to within 0.2 per cent. the percentage of methyl alcohol in acetone when the former varies between 4 and 20 per cent. (above the latter limit no experiments were carried out). When the percentage is below the former limit it can be determined approximately by comparing the color reactions with those produced by acetone containing known amounts of methyl alcohol and when the experiments are carried out under the same conditions.

As an alternative method, when results accurate to within 0.2 per cent. can be obtained, the acetone mixture containing the lower percentage of methyl alcohol can be mixed with one containing a known higher percentage, so as to being the total in the mixture to more than 4 per cent., and then carrying out the estimation of the methyl alcohol in this mixture by the method described in detail below, subsequently deducting the amount of added methyl alcohol from the result. A convenient method of carrying out the process is to add to the acetone-methyl alcohol mixture (containing the unknown amount of methyl alcohol) an equal volume of acetone containing 10 per cent. (by volume, as the specific gravities of methyl alcohol and acetone differ only very slightly) of methyl alcohol. By subtracting 5 from the percentage found in this mixture, and doubling the number thus obtained, the percentage of methyl alcohol in the mixture under investigation can be calculated.

The actual determination was carried out in the following manner: 5 Cc. of the acetone containing methyl alcohol under investigation were diluted to 250 Cc. with water. Quantities each of 5 Cc. of this mixture were introduced into a series of test-tubes ($6'' \times {}^{3}/_{4}''$) containing 5 Cc. of ammonium persulphate solutions of varying concentrations.

TABLE II.

Per Cent. MeOH in Methyl Alcohol Acetone Mixture.	Formaldehyde Reaction after Heating with Persulphate Solutions of the Following Concentrations.				
	5 Per Cent.	4 Per Cent.	3 Per Cent.	2 Per Cent.	1 Per Cent.
10	o	?	+++	+++++	+++++
9	o	?	+++	+++++	+++++
8	o	o	+	+++	+++++
7	o	o	?	+++	+++++
6	o	o	o	++	+++++
5	o	o	o	+	++++
4	o	o	o	?	+++
3	o	o	o	o	+++
2	o	o	o	o	+
1	o	o	o	o	?

The test-tubes were provided with corks containing short air-condensers, and were then introduced into a water bath containing boiling water in which they were kept immersed for ten minutes. At the end of this period each mixture was shaken, and the formaldehyde test was applied (using 1 Cc. of the hot solution) in the manner already given under the description of the determination of methyl alcohol in water. By using persulphate solutions of 1, 2, 3, 4, 5 per cent., an approximate estimation of the methyl alcohol can be made, as will be obvious from the table given above.

In the following table are given the percentages of persulphates in 5 Cc., which, when mixed with 5 Cc. of the diluted methyl alcohol acetone mixtures, just gave the positive reaction described above, which corresponds to the end-point.

TABLE III.

Per Cent. CH_3OH in Original Mixture.	Per Cent. Concentration of Persulphate in 5 Cc. Added.	Per Cent. CHOH in Original Mixture.	Per Cent. Concentration of Persulphate in 5 Cc. Added.
20.0	6.4	8	2.56
17.5	5.8	7	2.24
15.0	4.8	6	2.04
12.5	4.0	5	1.7
10.0	3.2	4	1.45
9.0	2.9	..	....

The above researches were carried out for the Food Investigation Board.

CONCLUSIONS.—(1) A method for estimation of methyl alcohol in water is described, the essential principle of which consists in determining the concentration of ammonium persulphate necessary to destroy completely the formaldehyde formed in the initial stages of the oxidation process under certain specified conditions of experiment. For the detection of formaldehyde the method previously described by one of the authors has been employed.

(2) By a slight modification of this method the amount of methyl alcohol in acetone can be estimated.

(3) To determine the amount of methyl alcohol in ethyl alcohol, the mixture of alcohols is partially oxidized by a relatively small amount of persulphate (the alcohols being in excess), and the formaldehyde formed under these conditions is estimated colorimetrically.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY.

THE NATURE OF THE FAT-SOLUBLE VITAMIN*

The discovery of the dietary importance of that property of many foods which is now termed fat-soluble vitamin or fat-soluble A represents a contribution of American physiologists[1] to the science of nutrition. It has been repeatedly verified both in this country and abroad. According to the observations made on a variety of experimental animals, the lack of the fat-soluble vitamin in the diet during adolescence may lead to an inhibition of growth together with symptoms of decline in health. Most conspicuous in a specific way is the apparently increased susceptibility to bacterial infection. In the case of rats this lowered resistance first betrays itself in many instances by the appearance of a characteristic disorder of the external eye which has provisionally been classed as a xerophthalmia. It usually begins with a swelling of the lids which is followed by an inflamed and catarrhal conditionof the conjunctiva. This rapidly becomes worse, and the discharge, which is at first hemorrhagic, frequently becomes purulent. If untreated, the cornea may become involved and total blindness result. If a food containing fat-soluble vitamin is administered, the symptoms usually clear up in a few days without further treatment, and growth is resumed. The same phenomena have been observed in mice, and more recently in rabbits kept on diets poor in the fat-soluble vitamin.[2] A possible relation of the lack of the latter to the occurrence of phosphatic calculi has also been pointed out by Osborne and Mendel.[3]

Whether and in what manner a dietary deficiency in fat-soluble vitamin plays a part in human disease remains to be ascertained. The probability of the need of this food accessory in the ration of man is large and the possible dire effects of a lack of it are being discussed widely at present, notably in relation to the pathogenesis of pellagra, rickets and xerophthalmia in childhood. The fact that many fats, such as lard, vegetable oils and hydrogenated fats, which have found widespread use in the dietary of man in recent years, are

* From the *Jour. Amer. Med. Assoc.*, Aug. 21, 1920.

[1] McCollum, E. V., and Davis, M.: *J. Biol. Chem.*, 15: 167, 1913; Osborne, T. B., and Mendel, L. B., *Ibid.*, p 311.

[2] Nelson, V. E., and Lamb, A. R.: "The Effect of Vitamine Deficiency on Various Species of Animals, I. The Production of Xerophthalmia in the Rabbit," *Am. J. Physiol.*, 51: 530 (Apr.), 1920.

[3] Osborne, T. B., and Mendel L. B.: "The Incidence of Phosphatic Urinary Calculi in Rats Fed on Experimental Rations," *J. A. M. A.*, 69: 32 (July 7), 1917.

virtually devoid of fat-soluble vitamin has caused some concern owing to the relatively high cost of those fats, like milk fat and egg fat, which are rich in it. It is a relief to know, however, that the fat-soluble vitamin has a far wider distribution in nature than the earlier studies led physiologists to suspect. Only recently the researches of McCollum, Steenbock and their collaborators at the University of Wisconsin, [1] and of Osborne and Mendel[2] in New Haven, have indicated the richness of many sorts of plant tissues in all familiar types of vitamins, thus placing the dietary importance of "vegetables" in a new light.

In commenting on this information, Osborne and Mendel remark that it emphasizes the use of vegetables to supplement the refined foods of the modern food industry which furnishes products rich in proteins, fats and carbohydrates, but in many cases comparatively deficient in the vitamins. The newly acquired facts, they add, serve as a further reminder that the fat-soluble vitamin need not be sought solely in foods known to be rich in fats. Fat-soluble vitamin has never been isolated, nor has it been concentrated in any way which avoids the simultaneous presence of ordinary fats, to some extent at least. Although its reactions and behavior toward solvents suggest a lipoidal character, Steenbock and Boutwell[3] have demonstrated that the fat-soluble vitamin resists saponification with alkalis whereby true fats are converted into soaps. Hence it can scarcely be regarded as identical with fats. This fact, for which some evidence had already been available, represents a distinct step in advance in the study of vitamins.

The extracts containing fat-soluble vitamin as obtained from natural products are invariably colored. Yellow corn is richer in fat-soluble vitamin than is white corn; there is a similar contrast be-

[1] Steenbock, H., and Gross, E. G.: "Fat-Soluble Vitamine, II. The Fat-Soluble Content of Roots, together with Some Observations on Their Water-Soluble Vitamine Content," *J. Biol Chem.*, 40: 501 (Dec.), 1919; "IV. The Fat-Soluble Vitamine Content of Green Plant Tissues, together with Some Observations on Their Water-Soluble Vitamine Content," *Ibid.*, 41: 149 (Feb.), 1920; McCollum, E. V.: "Newer Knowledge of Nutrition," New York, 1919.

[2] Osborne, T. B., and Mendel, L. B.: "The Vitamines in Green Foods," *J. Biol. Chem.*, 37: 187 (Jan.), 1919; "Nutritive Factors in Plant Tissues, IV. Fat-Soluble Vitamine," *Ibid.*, 41: 549 (Apr.), 1920.

[3] Steenbock, H., and Boutwell, P. W.: "Fat-Soluble Vitamine, VI. The Extractability of the Fat-Soluble Vitamine from Carrots, Alfalfa, and Yellow Corn by Fat Solvents," *J. Biol. Chem.*, 42: 131(May), 1920.

tween colorless lard and the yellow milk fat and egg fat. Hence Steenbock[1] has advanced the theory that the vitamin may be yellow pigment or at any rate a closely associated substance. His latest contribution is corroboratory; it also indicates that the vitamin attends the carotin rather than the xanthophyll variety of pigments, either or both of which may represent the yellow coloring matter in animal and plant foods. These findings, if they are further substantiated, mark a distinct step in advance toward the goal of discovering the nature of the fat-soluble vitamin.

SOME RECENT SAMPLES OF "GREY" CINCHONA BARK.*

By Bernard F. Howard, F.I.C., and Oliver Chick, A.I.C.

Grey Bark of Huanuco (a locality of Lower Peru) was a fairly common kind of Peruvian bark to be met with on the London market in the sixties and seventies, but, owing to its low quinine content and the severe competition of rich Java barks, its importation gradually diminished, and for the last twenty years, at any rate, it has been almost unknown as a bark of commerce.

The temporary shortage of cinchona due to the war, however, has caused it to reappear, and the authors have had the opportunity of studying several samples of good-sized parcels from the point of view of modern analytical methods.

The literature of Grey Bark dates almost entirely from the period mentioned above, botanically. Weddell, in his "Notes on the Quinquinas," published in 1871, p. 39, states that *Cinchona nitida* together with *C. Peruviana* and *C. micrantha*, supplies the market with "Quinquina gris," or grey bark, and it seems generally agreed among all experts that a normal sample of grey bark would be expected to contain these three varieties.

From the analytical point of view, most of the published work, dating back some fifty years or more, is necessarily vague, owing probably to the fact that the methods of separation and estimation of the various alkaloids in the bark were at that time very uncertain. J. E. Howard stated (Pereia, "Mat. Med.," Vol. II, Pt. II, p. 98, fourth edition) that he found "nearly twice as much

[1] Steenbock, H.: "White Corn *vs.* Yellow Corn and a Probable Relation between the Fat-Soluble Vitamine and Yellow Plant Pigments," *Science*, 50: 352 (Oct. 10), 1919.

*Reprinted from *The Pharmaceutical Journal and Pharmacist*, July 24, 1920.

cinchonine as quinine," and Delondre and Bouchard found cinchonine in relation to quinine sulphate in the proportion of 4 to 1.

From some old records of J. E. Howard it would appear that on analysis a typical grey bark of that period would yield about 0.45 per cent. quinine sulphate and about 0.90 per cent. cinchonine alkaloid. A parcel of thirty-eight bales, mark "D. F. C.," ex. s.s. "Cedric," was analyzed early this year, and the authors obtained the following results, which are fairly well in keeping with the references given above:

Quinine Alkaloid	0.45	per cent.
Cinchonidine Alkaloid	0.22	"
Cinchonine Alkaloid	0.63	"
Quinidine Alkaloid	nil	
Amorphous Alkaloid	0.48	"
Total Alkaloid	1.78	"

The selling analysis quoted by the merchant showed quinine 0.42 per cent., and total alkaloid 1.49 per cent., which closely agrees with the authors' fuller separation of the alkaloids given above.

Another parcel of "Loxa" bark recently analyzed, apparently of the same type, contained quinine alkaloid 0.33 per cent. and cinchonine alkaloid 0.58 per cent.

These two recent parcels appear to conform to the old standards of typical grey bark, and call for no special comment, but the following large parcel, the details of which are given below, is, in the authors' opinions, unique in the history of the Cinchonaceae.

In March, 1920, we received from the same source a sample of a parcel of 138 bales of South American cinchona bark (marked "D F. C.," ex. s.s. "Elder Branch"), together with an analytical report that it contained 6 per cent. of alkaloids, but only minute traces of quinine. The sample was therefore submitted to a very thorough examination, with most surprising results, which fully bore out the analyst's statement above mentioned:

Quinine Alkaloid	0.027	per cent.
Cinchonine Alkaloid	5.490	"
Amorphous Alkaloid	0.785	"
Total Alkaloid	6.302	"

There were evidences of very small quantities of quinidine, but apparently no cinchonidine was present.

In order to confirm the cinchonine value, the separated alkaloid was examined by the optical test, and gave exactly the correct value for α.

The bark was then submitted to Mr. E. M. Holmes for his opinion, and was reported as Grey Bark of Huanuco. The bulk of the sample consisted of *Cinchona nitida* (Pereira, "Mat. Med.," Vol. II, Pt. II, p. 98, fourth edition) and *Cinchona Peruviana* (J. E. Howard), together with a small amount of *Cinchona officinalis*. As mentioned above, grey bark as known on the market in the sixties and seventies usually contained the first two varieties, together with *Cinchona micrantha*, which was absent in the sample under examination. There would seem to have been some doubt in the past as to whether or not the *Peruviana* of J. E. Howard was identical with *Cinchona nitida* of Ruiz and Planchon, and in order possibly to throw some light on this point the first two varieties, as sorted out of the bulk sample by Mr. Holmes, were again examined analytically:

Cinchona Nitida.	Per Cent.	*Cinchona Peruviana,* Per Cent.
Quinine Alkaloid / Cinchonidine Alkaloid	0.20	0.28
*Cinchonine Alkaloid	5.08	5.04
Quinidine Alkaloid	Trace	Trace
Amorphous Alkaloid	0.82	1.28
Total Alkaloid	6.10	6.60

*The cinchonine was again checked by optical test, and gave a specific rotation of 208° and 212°, respectively, which is sufficiently close to Allen's figure of 226° for identification purposes.

The average of two tests (6.35 per cent.) confirms the first result of the samples as a whole (6.302 per cent.).

From the analytical point of view, therefore, the alkaloidal contents of the *Peruviana* was practically identical with the *Nitida*.

It therefore remained to compare the two barks, microscopically, and Mr. Holmes kindly undertook to have this examination carried out.

The authors feel that they cannot do better than give this report in full:

The microscopic examination of the bark indicates that it is in all probability a form of *Cinchona Peruviana*, Howard, remarkably rich in cinchonine, bearing somewhat the same relation to that species that *Cinchona Ledgeriana* does to *Cinchona Calisaya* Wedd.

The bark from which the sample was taken is evidently the bark recognized in commerce as Huanuco or Lima bark. This bark is stated by Pereira to be collected in Cuchero and Huanuco and exported from the Peruvian port of Lima (Callao). In his time, about 1857, two distinct barks were found to be mixed under this name, one referred to *Cinchona nitida* R. and P., and the other to *C. micrantha* Wedd., the *C. nitida* being distinguished as "fine grey bark" and the *C. micrantha* as "inferior or coarse grey bark" and (Pereira, "Mat. Med.," 4th Ed., 1857, Vol. II, Pt. II, p. 98, 99), but both of these barks were then imperfectly known. But the various species sent into commerce under the name of grey or Huanuco bark appear to have changed in course of time, for Vogl, "Pharmacognosie," p. 286, states that Huanuco bark was then (1896) derived from *C. macrocalyx*, mixed with a large proportion of the barks of *C. ovata* and *C. Peruviana*, but rarely with that of *C. micrantha*.

Planchon, "Drogues Simples," Vol. II, p. 124 (1896), states that the Huanuco bark was usually derived from three distinct species, viz., *Cinchona nitida* R. and P., *C. micrantha* R. and P., and *C. Peruviana* How., the first named being then very rare, and *C. Peruviana* constituting the principal portion of Huanuco bark. Fortunately, he gave two illustrations of the microscopic structure of *C. nitida* and *C. Peruviana* How., that of *C. nitida* agreeing fairly well with the illustration of that bark in Berg's "Anatomischer Atlas," published in 1865. taf. 34, No. 80, where an illustration of *C. micrantha* is also given on the same page, No. 82. Berg, however, expressly states that the *C. nitida* he illustrates is not that described by J. E. Howard, but is the *C. nitida* of Ruiz and Pavon, is the *Cascarilla Peruviana* of Pavon. Like that of Planchon, the illustration indicates the absence of laticiferous vessels and stone cells in the cortical parenchyma, while they are abundantly present in Planchon's *C. Peruviana*. This species, however, is not given in Berg's atlas. These two features are also absent from the illustration of *C. micrantha* given by Berg.

The specimen of Huanuco bark recently received from B. F. Howard is seen under the microscope to consist chiefly of bark belonging to the group in which laticiferous cells and sclerenchymatous cells are distributed through the cortical parenchyma. This group includes *Cinchona ovata, C. Pelleteriana, C. Peruviana, C. purpurea* and *C. umbellifera*. The bark in question must therefore

belong to one of these species or to an undescribed species belonging to the same group.

Of those Cinchonas to which Huanuco bark has been attributed by different authorities, *C. micrantha* and *C. nitida* are excluded by reason of containing neither laticiferous vessels nor sclerenchymatous cells in the cortical parenchyma; also *C. macrocalyx* because although it shows sclerenchymatous cells it has no laticiferous vessels. The choice of known species rests, therefore, between those of the group just mentioned. Of these, *C. umbellifera* is characterized by having very few sclerenchymatous cells and a resinous zone under the periderm, and very small bast cells, somewhat regularly but radially arranged in narrow lines, and the cells of the medullary rays are represented as broader than long. According to Berg, this species is found abundantly in Huanuco bark.

In *C. ovata* the cork consists of colorless, not brown, cells. This bark may be, therefore, left out of consideration, as in Mr. B. F. Howard's bark they are dark brown.

C. Pelleteriana has liber cells varying much in diameter, and also shows club-shaped liber cells (stabformig) in the bark, and it is not known to occur in Huanuco bark.

C. purpurea has also a pale cork like *C. ovata*. Like *C. Pelleteriana*, it contains club-shaped liber cells. It is sometimes found in Huanuco bark, but the pale cork distinguishes it from the bark under consideration.

C. Peruviana is not described by Berg, but is described by Vogl, *Loc. cit.*, p. 287, 288, and also by Planchon, who gives an illustration of it (*Loc. cit.*, p. 125). It is characterized by Vogl as having numerous club-shaped liber cells and crystal cells and the laticiferous cells often filled with thyllae. The laticiferous vessels form a single or double ring. The external appearance of this bark is described by Vogl as of a prevailing grey-brown color with yellowish, greenish, and whitish patches, with distant transverse cracks and well marked long fissures, and is of a cinnamon-brown color on the inner surface.

Planchon and Collin, *Loc. cit.*, p. 124, state that the small quills of *C. Peruviana* have a finely cracked periderm of a grey or slightly bluish tint and closely adherent to the liber, the transverse cracks being few and shallow. The larger quills always present a more or less dark grey tint and are characterized by the presence of white patches and longitudinal depressions, which are more or less clearly

marked. The transverse cracks often extend nearly round the large quills. The microscope shows a thick layer of cork cells, isolated sclerenchymatous cells in the cortical parenchyma, and the liber fibers are mostly isolated and arranged in radial lines.

The specimens received from Mr. B. F. Howard consist mainly of pieces of bark exhibiting the characters attributed to *C. Peruviana* How., by Planchon and Collin, and show the anatomical structure of that bark as illustrated and described by those authors and also as described by Vogl. Some of the pieces differ in the greater number of sand cells and in the smaller number of the stone cells in the cortical parenchyma.

The larger percenatge of cinchonine found in this shipment of Huanuco bark may possibly be due to the elevation at which the trees grow, as this factor and the accompanying differences of heat and moisture are known to influence the character of the alkaloids present. In the present state of our knowledge of the species of the Cinchona genus occurring in Peru I can only come to the conclusion that the bark submitted to me for examination is the produce of one, or possibly more, forms of *C. Peruviana* How., as interpreted in the illustration given by Planchon and Collin and Berg.

The authors were at a loss to understand the presence of *Cinchona officinalis* in a grey bark, and they also considered that if this variety were present in any quantity it would inevitably affect the alkaloidal contents. As has been shown above, *nitida*, *Peruviana*, and *micrantha* have always appeared to yield an exceptionally large amount of cinchonine, and this peculiarity has never been known to occur in the much less rare *officinalis* bark.

In order to establish the presence or otherwise of "*officinalis*" in this parcel, a fresh sample was drawn from the bulk, and again submitted to Mr. Holmes for his opinion. In this fresh sample he could find no *C. officinalis*, but classified it into three varieties. *nitida*, *Peruviana*, *micrantha*, together with another variety somewhat resembling *Pitayensis*, and which might either belong to this or the *Lucumaefolia* variety, or might possibly be a new variety altogether. From this examination it is fair to assume that the presence of a small quantity of *officinalis* in the first sample was purely accidental and not typical of the parcel, and that the amount was so small that it did not affect the unusual distribution of alkaloids.

The analyses of the varieties, as identified by Mr. Holmes, were as follows:

	C. Micrantha. Per Cent.	*C. Nitida.* Per Cent.	*C. Peruviana.* Per Cent.
Quinine Alkaloid } Cinchonidine " }	0.08	0.05	0.11
Cinchonine "	4.49	5.64	5.12
Quinidine "	trace	trace	trace
Amorphous "	0.33	0.30	0.50
Total Alkaloid	4.90	5.99	5.73

The amount of the obscure variety resembling *Pitayensis* was not sufficiently large to warrant a separate analysis, and it was considered important to preserve it intact as a specimen for future reference.

Mr. Holmes has expressed the opinion with regard to this exceptional parcel of grey bark that the abnormally high proportion of cinchonine indicates growth at a low elevation and a hot, moist atmosphere, basing his assumption on a statement by J. E. Howard (*Pharm. Journal*, 1883, XIII, p. 1013), that under these circumstances cinchonine is increased and quinine decreased.

Mr. Holmes also compares the contents of this sample with the well-known *Ledgeriana* variety of *Cinchona Calisaya*, in which quinine alone is present up to a high percentage (the present authors have analyzed samples of this bark containing up to 12 per cent. of quinine, expressed as sulphate) and the other alkaloids only in very small proportions. He also puts forward the extremely interesting supposition that if, under peculiar circumstances of cultivation, a variety of *Calisaya* bark can be produced with such a large proportion of quinine, so in the case of *Cinchona Peruviana* or *C. nitida* it is equally possible that under favorable conditions a variety should be found in which the high cinchonine value peculiar to this species is exaggerated almost to the point of extinction of the other alkaloids.

If this interesting supposition is accepted it goes far to account for the peculiar contents of the samples under discussion which at first sight seems almost inexplicable.

For many years past the commercial value of bark for manufacturing purposes (as distinct from druggists' bark) has been based almost entirely on the percentage of quinine present, but quite recently the great stimulation of interest in the hydrogenated derivatives of the various natural alkaloids has caused the distribution of the other principal bases, such as cinchonidine, cinchonine,

and quinidine in the bark, to be a matter of some importance and consequently any information regarding the conditions under which Nature herself tends to "separate" particular alkaloids in various species of Cinchona may be of considerable commercial value in the future, and not merely a question of academic interest.

The authors have made free use of the very valuable report and suggestions of Mr. Holmes, and it is partly at his request that this note is brought before the Conference.

THE SPREAD OF NOXIOUS PLANTS.*

Considerable consternation has been caused in the neighborhood of Wagga (N. S. W.) by the discovery that St. John's Wort has taken a firm hold of certain parts of the district, and threatens to render valueless a considerable tract of country if its spreading cannot be prevented. There are several parts of the commonwealth in which this pest has taken such a hold that cultivation has become a difficulty, and the native herbage has been destroyed by the invader.

The *Hypericum perforatum* has long been esteemed in medicine, and was formerly official in the French Codex. It is still esteemed among herbalists in the United States as a stimulating expectorant and emmenagogue, and a diuretic, as well as a local application for local pains, contusions, and burns. It is said to have been first introduced into Victoria by a German woman who practiced as a herbalist, and who cultivated it for medicinal purposes. It has spread to an alarming extent, and the Pastures Protection Board of the Wagga district are taking vigorous steps for its eradication, and to prevent it spreading to district lands. The weed was discovered growing by the roadsides and in vacant blocks of land, and the town council have been urged to take immediate steps to prevent its further spread.

Mr. J. H. Maiden, F.R.S., Director of the Sydney Botanic Gardens, recently offered to supply persons desirous of obtaining the seeds of the red poppy gathered in the Somme valley battlefields, and from the school children of Villers-Brettoneux with small quantities of this seed for garden cultivation, to remind them of the brave soldiers who fell there. This was met with a vigorous protest and the statement was made through the columns of the daily press that we have quite enough noxious plants and animals in New South

* From the *Australasian Journal of Pharmacy.*

Wales without adding to the number the French red poppy, which, like the Scotch thistle, may first be cultivated as a garden plant, but on being allowed to spread may prove difficult of eradication. The lantana or Cape stink weed is an evidence of the danger that may arise from the introduction of a flowering plant into a climate and country particularly suitable for its propagation. The foxglove has become a noxious weed in New Zealand, and among the tobacco crops of New England there has been a difficulty in eradicating the henbane. Sweet fennel is classed among the noxious plants by the Department of Agriculture of this state, and its cultivation is prohibited.

Mr. C. G. Orr, pharmacist, of Port Macquarie, has been experimenting in growing several tropical plants, and is said to have met with considerable success in the cultivation of the Cavendish banana and the pineapple. Mr. George Turvey is another pharmacist who has been studying the cultivation of medicinal plants on his allotment at French's Forest. The work of Mr. Orr has been favorably commented upon by the agricultural editors of the daily press.

F. W.

THE PURIFICATION OF CRUDE COCAINE.*

The separation of the various bases obtained during the process of extracting coca leaves with sodium carbonate and petroleum ether has been made the subject of an exhaustive study by Dr. L. R. de Rosemont, of the University of Geneva (*Jour. Suisse de Pharm.*, April 29, 1920). He first established the solubility of the various bases in different solvents, and found that cocaine, cinnamyl-cocaine, isococaine, and isotropyl-cocaine were all easily soluble in ether, alcohol, chloroform, ligroin, and benzene. Crude cocaine is partly soluble in water, and contains about 10 to 13 per cent. of sodium carbonate and bicarbonate, in addition to chlorides and alkaline sulphates.

Dr. de Rosemont describes twelve different methods he investigated for obtaining pure cocaine, including a study of the processes described in four German patents. The process he considers best (it yields from 79 to 81 per cent. of chemically pure cocaine) is as follows: Ten grams of crude cocaine is dissolved in hot water containing 5 grams of β-naphthalene-sulphonic acid, and the solution

* From *The Chemist and Druggist*, July 3, 1920.

is filtered while warm. On cooling it deposits an oily-resinous body which soon becomes a semi-crystalline mass. Ammonium carbonate is added until the solution becomes cloudy, then solution of ammonia, which produces a beautiful white precipitate. This is extracted with ether and the pure cocaine crystallizes out from the ethereal solution. The β-naphthalene-sulphonic acid may also be recovered by concentrating the mother liquors and precipitating with hydrochloric acid.

Another process recommended by the author consists in dissolving 10 grams of crude cocaine in boiling water containing acetic acid. On cooling, the solution is precipitated by the addition of ammonium carbonate, which yields a resinous, yellowish precipitate, lighter than water. The solution is filtered and solution of ammonia added in excess, the almost chemically pure cocaine which is precipitated is extracted with ether, from which it crystallizes spontaneously. This method also yields 79 to 81 per cent. of chemically pure cocaine. In addition to separating the cocaine from the crude product, the author also dealt with the question of utilizing the residue (*i. e.*, the resinous precipitate first thrown down) obtained in the course of precipitating the pure alkaloid, particularly the possibility of transforming the ecgonine present in this residue into cocaine. This residue is purified by crystallization from alcohol, and pure ecgonine is precipitated afterwards by means of carbonate of sodium. The pure ecgonine thus obtained is then dissolved in methyl alcohol, and the solution treated with anhydrous hydrochloric acid, yielding methyl-ecgonine hydrochloride; the unaltered ecgonine is then extracted with ether. Of the methyl-ecgonine thus obtained, 20 grams is heated on a water bath with benzoyl chloride 20 grams, until no more hydrochloric acid is evolved. The solution is now added to cold water, whereby benzoic acid is precipitated; this is filtered out and the filtrate concentrated. The synthetic cocaine (termed coca-ethyline in the German patent 47,713) is then precipitated from the filtrate by the addition of solution of ammonia. By this method of treating the residue a further yield of 5 to 10 per cent. of cocaine is obtainable.

RAT POISONS.*

Phosphorus, arsenic, and strychnine, says Mr. Thomas Parker, F.R.C.V.S., in a paper published in *The Veterinary Journal*, are often used in the preparation of rat-pastes or vermin killers, but, as they are all rapidly fatal in their effects on man and the domestic animals, and therefore dangerous, are not recommended. There are others which, while being rapidly fatal to rats, are comparatively harmless to domestic animals. These are barium carbonate and squill.

Barium Carbonate.—Although $1^1/_2$ to 2 grains suffices to kill a rat, barium carbonate is more or less harmless to domestic animals, cats and chickens withstanding 10 to 15 grains, and an average-sized dog over 100 grains. It has also the advantage of being cheap, tasteless, odorless, and therefore easily made attractive by mixing with a suitable bait, and has been found to be as effective as the more dangerous poisons, such as phosphorus and arsenic. The bait may be prepared in the following manner: Make a paste by well mixing equal parts of the powdered barium carbonate and tallow-fat or dripping, and spread it over thin slices of bread exactly as one would do with butter. Then, having firmly pressed the slices together to form sandwiches, they are cut into small squares ready for use. Of course, it may be mixed with any other bait found equally or more acceptable. Owing to the action of barium carbonate on the lining membrane of the stomach the rats are induced to leave their holes in search of drink. It is recommended, therefore, to place within reach on the day following the treatment, shallow bowls containing a solution consisting of equal parts of liquid squill and milk, the rats being thus made to partake of more poison in their efforts at relief.

Squill may be obtained either in the form of a powder or of a solution. Although comparatively harmless to domestic animals, it is extremely toxic as far as rats are concerned, the minimum lethal dose being only half a grain. Mix the powdered squill with tallow or dripping, or with either of these fats and oatmeal. The mixture should be smeared on bread, the latter being then cut into small pieces. In the liquid form squill may be prepared for use in the following manner: Mix equal parts of liquid squill and milk, and to each pint of the solution add 1 lb. by weight of bread.

Of all rat poisons squill solution is believed to be the most effective, and has been recommended in preference to barium carbonate for the following reasons:

* From *The Australasian Jour. of Pharm.*, June 21, 1920.

(*a*) It is three times as toxic for rodents.

(*b*) It is even less harmful to most domestic animals.

The one point against the use of squill, however, lies in the fact that at present it is somewhat more expensive than most other poisons.

There is always a possibility of a rat dying under flooring or behind wainscoting, either through poison or otherwise. If a rat from a drain takes poison and cannot regain its habitation, the carcass will most probably become putrid. If such a rat dies near a fireplace or hot-water pipe, the stench will be intensified. Chloride of zinc is a good deodorizer in such cases, and combines with and neutralizes the offensive chemical products of putrefaction. If necessary, a hole should be bored with a bit and brace in the vicinity of the supposed source of origin of the odor if possible. Some perfume or pinewood oil can be added to the zinc chloride, which should be applied through the hole. A cork will close the orifice, and can be withdrawn from time to time to ascertain whether the nuisance has abated. Where possible, however, it is advisable to remove the carcass immediately its presence has been detected.

THE CHEMISTRY OF ODORS.*

Man and animals alike depend on their senses not only for physiologic delight but also for the warnings against various dangers of their environment. The "twin senses" smell and taste exercise a peculiarly valuable function in that they stand "like sentries at the portals of the body, where they closely scrutinize everything that enters." Slosson[1] has fancifully remarked that these two special senses lead us to the heart of the molecule and enable us to tell how atoms are put together. Sounds and sights may be disagreeable, but they are never fatal. A man can live, Slosson writes, in a boiler factory or in a cubist art gallery, but he cannot live in a room containing hydrogen sulphide. Until recently there has been little dependable information available about the chemical nature of the odoriferous substances encountered in daily life. The so-called essential oils, many of which have a "fruity" odor, have been prepared for some time in the laboratory. Experts remind us, however, that the artificial fruit essences are usually composed of a mixture of substances without any guarantee of their actual occurrence in the fruits whose

* From *Jour. Amer. Med. Assoc.*, Aug. 14, 1920.

[1] Slosson, E. E.: "Creative Chemistry," New York, The Century Company, 1920.

flavors they are supposed to represent. An actual identification of the principal flavoring constituent of an edible fruit was apparently first accomplished in 1913 by Kleber,[1] who showed by accurate methods that ripe bananas actually contain amyl acetate, the substance commonly designated as "pear oil." Recently Power and Chestnut[2] of the Bureau of Chemistry in the U. S. Department of Agriculture at Washington have unraveled some of the mysteries of the apple. They obtained no evidence that amyl valerate, familiarly designated as "apple oil," is present in the fruit. Its odorous constituents were found to consist essentially of the amyl esters of formic, acetic and caproic acids, with a very small amount of the caprylic ester and a considerable proportion of acetaldehyde. It is not unlikely that some of the alcohol and acids mentioned are also present in the free state. All of these various substances occur in mixtures of varying proportions in the numerous varieties of the apple, thus giving rise to slight differences of odor. The quantities actually present, for example, 0.0007 per cent. in the Ben Davis and 0.0013 per cent. of essential oil in the more odorous crab-apple, may seem small. Nowadays, however, the physician who deals with antigens and antitoxins, with radium, with vaccines and vitamins, has become accustomed to the possible potency of products in small quantities.

INTERNATIONAL ATOMIC WEIGHTS, 1921.*

The report of the International Committee on Atomic Weights is given in the following table:

	Symbol.	Atomic Weight.		Symbol.	Atomic Weight.
Aluminum	Al	27.1	Calcium	Ca	40.00
Antimony	Sb	120.2	Carbon	C	12.005
Argon	A	39.9	Cerium	Ce	140.25
Arsenic	As	74.96	Cesium	Cs	132.81
Barium	Ba	137.37	Chlorine	Cl	35.46
Bismuth	Bi	208.0	Chromium	Cr	52.0
Boron	B	10.9	Cobalt	Co	58.97
Bromine	Br	79.92	Columbium	Cb	93.1
Cadmium	Cd	112.47	Copper	Cu	63.57

[1] Kleber, C., *Am. Perfumer*, 7: 235, 1913.

[2] Power, F. B., and Chestnut, V. K.: "The Odorous Constituents of Apples; Emanation of Acetaldehyde from the Ripe Fruit," *J. Am. Chem. Soc.*, 42: 1509 (July), 1920.

**Journal Amer. Chem. Soc.*, Sept.

	Symbol.	Atomic Weight.		Symbol.	Atomic Weight.
Dysprosium	Dy	162.5	Phosphorus	P	31.04
Erbium	Er	167.7	Platinum	Pt	195.2
Europium	Eu	152.0	Potassium	K	39.10
Fluorine	F	19.0	Praseodymium	Pr	140.9
Gadolinium	Gd	157.3	Radium	Ra	226.0
Gallium	Ga	70.1	Rhodium	Rh	102.9
Germanium	Ge	72.5	Rubidium	Rb	85.45
Glucinum	Gl	9.1	Ruthenium	Ru	101.7
Gold	Au	197.2	Samarium	Sa	150.4
Helium	He	4.00	Scandium	Sc	45.1
Holmium	Ho	163.5	Selenium	Se	79.2
Hydrogen	H	1.008	Silicon	Si	28.3
Indium	In	114.8	Silver	Ag	107.88
Iodine	I	126.92	Sodium	Na	23.00
Iridium	Ir	193.1	Strontium	Sr	87.63
Iron	Fe	55.84	Sulphur	S	32.06
Krypton	Kr	82.92	Tantalum	Ta	181.5
Lanthanum	La	139.0	Tellurium	Te	127.5
Lead	Pb	207.20	Terbium	Tb	159.2
Lithium	Li	6.94	Thallium	Tl	204.0
Lutecium	Lu	175.0	Thorium	Th	232.15
Magnesium	Mg	24.32	Thulium	Tm	168.5
Manganese	Mn	54.93	Tin	Sn	118.7
Mercury	Hg	200.6	Titanium	Ti	48.1
Molybdenum	Mo	96.0	Tungsten	W	184.0
Neodymium	Nd	144.3	Uranium	U	238.2
Neon	Ne	20.2	Vanadium	V	51.0
Nickel	Ni	58.68	Xenon	Xe	130.2
Niton (radium emanation)	Nt	222.4	Ytterbium (Neoytterbium)	Yb	173.5
Nitrogen	N	14.008	Yttrium	Yt	89.33
Osmium	Os	190.9	Zinc	Zn	65.37
Oxygen	O	16.00	Zirconium	Zr	90.6
Palladium	Pd	106.7			

THE MEETING OF THE AMERICAN CHEMICAL SOCIETY.

The semi-annual meeting of the American Chemical Society, held at Chicago during the week of September 6th, was rich in achievement and splendidly attended. Over twelve hundred members representing every section of the country were in attendance.

As usual, all of the business of the Society was transacted by the Council, which met Monday afternoon and evening, September 6, at the University Club. The most important matters of business transacted were: Changing the name of the Division of Pharma-

ceutical Chemistry to Division of Chemistry of Medicinal Products; changing the name of the Carney's Point Section to South Jersey Section; going on record as favoring the purchase of Liberty Bonds for investment purposes; fixing the date of the spring meeting at Rochester, N. Y., for the week of April 25th; selecting Pittsburgh as the fall meeting city unless arrangements can be made for a joint meeting of the Canadian and British Societies of Chemical Industry with the American Chemical Society at New York either preceding or following the Chemical Exposition in New York next September; cautioning local sections of the Society against affiliations with local engineering organizations which may involve the parent body in matters of public policy favored by engineers but not of interest to chemists; re-election of the present editors of the three journals of the Society to serve for one year; authorizing the appointment of a committee of thirteen to coöperate with the Chemical Warfare Service along lines of research, development, production and physiological questions; re-endorsing the position taken at the last meeting in favor of the dyestuffs protection bill still before Congress; increasing the annual dues from $10 to $15 with the proviso that undergraduate and graduate students may secure such membership for $10 per annum.

Meetings of the various divisions of the Society were held at the University of Chicago, Wednesday and Thursday, September 8 and 9.

The program of the Division of Chemistry of Medicinal Products included papers on the newer anti-spasmodics of the benzyl benzoate type. Reports were made by various investigators on benzyl succinate, benzyl esters of salicylic acid, and benzyl esters of the higher fatty acids. There seemed to be an undercurrent of opinion that benzyl benzoate could be improved upon and it is evident that many manufacturers are engaged in research work along this line.

An entire afternoon was devoted by this section to a discussion of methods of coöperation with the National Research Council. Dr. Wilder D. Bancroft, of the Council, advocated the framing of a complete program of research along medicinal chemical lines, after which the aid of the Council could be counted upon in carrying out the work outlined. Dr. C. H. Herty expressed the hope that an institute for research, along the lines of developing synthetic medicinal compounds, be organized in the near future and mentioned the possibility of securing financial aid for this purpose through the Chemical Foundation. After considerable discussion on this subject

it was decided to appoint a committee to digest the papers and viewpoints expressed at this meeting and formulate some definite plan of research. The following committee was appointed: J. M. Francis, chairman; F. R. Eldred, Edward Kremers, Mr. St. John and H. V. Arny.

The question of controlling the entry of narcotic drugs through Pacific Coast ports was also discussed and the following committee appointed to consider the matter and report to the Board of Directors of the Society: Prof. W. F. Rudd, chairman; E. R. Carter and F. R. Eldred.

The division re-elected Dr. C. E. Caspari, of St. Louis, chariman, and Edgar R. Carter, of Indianapolis, secretary. Other officers elected were W. F. Rudd, vice-chairman; Messrs. Taylor and R. P. Fischelis, members of the executive committee.

The Society held several general sessions at which papers of popular as well as scientific interest were presented, the presidential address of Wm. A. Noyes on "Chemical Publications" being of particular interest.

The entertainment features were elaborately planned and well executed, a notable feature being the many visits to various industrial institutions in and near Chicago. R. P. F.

THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.

ABSTRACTS FROM THE MINUTES OF THE SEMI-ANNUAL MEETING.

The semi-annual meeting of the Philadelphia College of Pharmacy and Science was held September 27, at 3 P.M. President Howard B. French presided and thirty members were present.

The amendments to Article I of the Constitution and Article XII of the By-Laws as presented at the June meeting, were read and adopted.

The report of the Committee on Nominations was presented.

Dr. Robinson for the "Medical Section of the Alumni," reported that a preliminary meeting had been held, views exchanged and various plans proposed—one most favorably received was to have a luncheon in the near future and then organize for effective work.

Joseph W. England reported for the Committee on Memorial Resolutions on the decease of Edwin M. Boring; reported they had

completed their work and the engrossed resolutions were on the table for the inspection of the members.

George M. Beringer reported that the family of Mr. Boring had donated to the College almost a complete set of the AMERICAN JOURNAL OF PHARMACY, and moved that the thanks of the College be tendered for this valuable donation. So ordered.

Election of Trustees.—Messrs. Stewart, Gano and Harrison were appointed tellers.

The Committee on Nominations in submitting a list of nominees made the following statement: "Owing to the Amended Charter taking effect at this election, your committee, acting under instructions from the solicitor of the College, Edgar S. McKaig, Esq., asked for and received resignations from nine members of the Board of Trustees to take effect September 27. This was done to conform to the decree of the court by making it possible to elect twelve members of the Board of Trustees at this election." (Twelve more are to be elected in March, 1921, when the resignations of the remaining six members of the old Board of Trustees will be asked for.)

These nine resignations and three whose terms had expired September 27 (together with an unexpired term caused by death) created thirteen vacancies, to be filled by electing five for one year, four for two years, and four for three years.

While the ballots were being counted, Prof. E. F. Cook, the Executive Secretary of the Centennial Committee submitted a lengthy report of the work that had been done, an abstract of this report is given.

The Executive Chairmen are:

On Site, President Howard B. French.

On Contributions, Dr. R. V. Mattison.

On Historical Data and Centennial Volume, George M. Beringer.

On College Membership, J. C. Peacock.

On Publicity, Robert P. Fischelis.

Each of these chairmen will be supported by a committee which is yet to be announced.

The General Committee on the Centennial, so far as arranged, is as follows:

All officers of the College.

All members of the Board of Trustees.

All members of the Faculty.
Pharmacists: Men, M. D. Allen.
Women, Mrs. W. E. Lee, Mrs. C. H. LaWall.
Army, To be selected.
Navy, Dr. W. T. Minnick.
Physicians, Dr. W. D. Robinson.
Wholesale Druggists, Walter V. Smith.
Chemical Manufacturers, Dr. George D. Rosengarten.
Pharmaceutical Manufacturers, Milton Campbell.
Editors and Journalists, E. G. Eberle.
Analytical Chemists, Charles E. Vanderkleed.
Members of the State Boards of Pharmacy, L. L. Walton.
Salesmen, To be selected.
Students, To be selected.

The president of the college is to be chairman of this General Committee.

The United States has been divided into districts. Some states will have one district, some two districts, some three districts. Pennsylvania will have many districts, as also Philadelphia.

As the campaign develops and sufficient publicity material has been issued from the central office, the district committees will be asked to do some local work, and in the final month will be expected to make personal visitations, as far as possible, in an effort to secure contributions. Posters, descriptive booklets, circulars or other booklets will be issued.

Alumni Addresses.—In January of last year a request was sent to all alumni asking for biographical sketches. About 1800 were returned; a second appeal brought about 800 more. There are about 500 sketches received about 10 years ago. Many of these are no longer living. The material, however, is most valuable for the Historical Volume. There is a total of about 5,000 graduates from whom addresses are available, but the biographical sketches received represent only about one-half of this number.

Centennial Week.—It is proposed that Commencement Week in 1921 will be utilized for the Centennial celebration. The Pennsylvania Pharmaceutical Association meets in Philadelphia during the same week. A dinner at which class ogranizations will be present in large numbers will probably be a leading feature of the week's celebration.

Site.—The Committee have had the question of site under careful consideration, and it is hoped will be ready to report specifically in a short time.

The report was ordered entered and filed.

The deaths of Richard W. Cuthbert, a member of the College since 1872, and of Miss Jamella Fox since 1918, were announced.

George M. Beringer offered the following as a minute expressing the position of the College on the subject of illicit sales of narcotic drugs and alcoholic beverages and moved that it be adopted, spread upon our minutes and copies sent to the Government officials charged with enforcing the laws and to the medical and pharmaceutical press and to the newspapers.

The correction of alleged abuses in the drug and apothecary business was the principal reason assigned for the meetings of Philadelphia apothecaries in historic Carpenters Hall in 1821, that resulted in the incorporation of the Philadelphia College of Pharmacy. Since its inception this institution has always maintained the highest ideals of the moral obligation and the professional responsibilities devolving upon pharmacists, in the discharge of their duties to society. It has aimed to inculcate in its students and members a code of ethics in keeping with these ideals.

The laws enacted by Congress and the various Legislatures for the purpose of limiting the sale and dispensing of narcotic drugs and alcoholic beverages to strictly medicinal uses, have placed additional and grave responsibilities upon the pharmaceutical profession and the drug trade. Alcohol is the most important raw material of the drug and chemical industries and of necessity, in one way or another, enters into practically every operation of the pharmacist. It is the opinion of this College that the dispensing of all potent drugs, including narcotics and alcoholics, should be restricted to bona fide medicines and that the distribution of these should be exclusively a part of the professional duty of registered pharmacists.

The Philadelphia College of Pharmacy and Science realizes that with its amended charter and wider educational scope it retains fully its position of responsibility as the oldest pharmaceutical society in America and as a leading exponent of professional pharmacy. *Be it Resolved*, by the members in meeting assembled that they call upon every pharmacist to maintain faith with the Government and to demonstrate by his strict observance of the narcotic

and prohibition laws that the confidence of Congress and of the Legislatures in the integrity and honor of the pharmaceutical profession has not been misplaced. We denounce infractions of these laws not only as a menace to public welfare but likewise as inimical to our entire profession and believe that the violators who thus debase their calling merit the extreme penalties of the law and elimination from pharmaceutical associations and practice.

Dr. P. S. Stout added that the physicians present endorse these resolutions and pledge hearty coöperation in carrying out the provision mentioned, and the resolutions were unanimously adopted and directed to be given the widest publicity.

Prof. C. B. Lowe for Mr. E. S. Gatchell presented a copy of the first edition of the United States Dispensatory. The thanks of the College were voted to the donor.

The tellers reported as the result of the election for trustees that W. Duffield Robinson, George M. Beringer, Jacob M. Baer, Richard M. Shoemaker and H. K. Mulford had been elected for one year, and Joseph W. England, Otto Kraus, O. W. Osterlund and Samuel P. Sadtler had been elected for two years, and Wm. L. Cliffe, Russell T. Blackwood, Benjamin T. Fairchild and Walter A. Rumsey had been elected for three years.

Prof. LaWall, for Mr. Norman Dean, presented several old articles of pharmaceutical apparatus to the College. A vote of thanks was tendered the donor.

C. A. WEIDEMANN, M.D.,
Secretary.

CURRENT LITERATURE.

SCIENTIFIC AND TECHNICAL ABSTRACTS.

DISTRIBUTION AND MIGRATION OF COPPER IN PLANT TISSUES.—Copper is universally distributed in all plants. By means of the very delicate zinc-copper ferrocyanide reaction the authors have been enabled to follow its distribution in various organs of the same plant. As the result of a great number of determinations on nearly thirty different species, including common trees, shrubs, culinary vegetables, fruits, and herbs, it is found that copper occurs in all parts of the plant. At the same time, it is not evenly distributed, but is found on those parts which possess the highest vital activity. Speaking generally, apart from the process of ripening of the seed,

the organs which dry up in the process of aging part with a considerable portion of their copper, which is transferred to the actively growing tissues with the reverse material. Thus, in shrubs and trees the buds are richer in copper than the wood or the bark. In evergreens the fresh younger leaves contain more copper than the older leaves. It is, moreover, evident that this increase of copper is not due merely to concentration of the juices by evaporation. In this respect the accumulation of the metal in certain organs is of quite a different order from that of the increase of certain inorganic salts, such as silica and calcium compounds. In the case of the ripening of fruits there is an evident concentration of copper in the seeds. In leguminous plants the amount of copper present in the green immature seeds is notably greater than that in the pericarps. As ripening proceeds this increase becomes more and more evident in the former. This is directly opposite to what is observed in the case of calcium salts, wnich are found to accumulate in the pericarps and also in dead or mature leaves. Moreover, more copper is found in the albumen or the decorticated cotyledons than in their envelopes; in the kernel than in the shell of nuts; and in the seeds than in the pulp of fleshy fruits. All these facts are in agreement with what is observed during the period of growth, when copper is transferred to the most active tissues. It would appear, therefore, that copper is in some way intimately connected with the vital processes of the plant. At present it is not possible to state what part the metal may play; but the inference is permissible that it is not unimportant.

(L. Maquerme and E. Demoussy, *Comptes rend.*, 170:87, 1920; through *The Pharm. Jour. and Pharm.*, April 17, 1920.)

Staining Technic for Malaria Plasmodium.—Gutiérrez describes experiences with the different staining methods in vogue to decide which method is the most practicable and reliable. His final conclusion is in favor of the Tiedmann technic, slightly modified. A 1 per cent. solution of methylene blue in methyl alcohol is made, and a similar solution of eosin, and these are kept in dark colored vials. When ready to use, 10 Gm. of each solution and 10 Gm. of methyl alcohol are mixed, and 10 or 15 drops of the reagent mixture are poured on the smear of blood dried in the air. Then 20 or 30 drops of neutral, filtered water are added immediately, and the slide is tilted to insure the complete blending of the stain and the water. In one and one-half minutes—counting from the moment

the stain had been dropped on the specimen—the preparation is rinsed rapidly with water and dried with blotting paper, when it is ready for examination under the microscope. The water used does not have to be distilled water but it must be neutral; he prefers rain water for the purpose. Filtered water from any source can be used, provided that it is neutral. He tests for this by adding a small amount of pulverized hematoxylin to a test-tube containing 100 Cc. of the water and agitating gently. If the water turns yellow, this shows acidity, while a deep violet tint indicates that it is alkaline. A light violet tint indicates that the water is neutral and suitable to use. By adding a few drops of a 1 per cent. solution of sodium bicarbonate to the water and then a little more hematoxylin, comparing the tint with a control tube, the neutral reaction can soon be realized. This staining technic shows up all the forms of the plasmodium of malaria and other parasites of the blood, and it is excellent also for the differential leukocyte count. In conclusion he emphasizes that with this simple and reliable technic any practitioner can examine blood specimens, himself, without expensive equipment or relying on a distant laboratory. (From *Porto Rico Medical Assoc. Bulletin, San Juan,* Mar. 1920, 14, No. 125; through *Jour. Amer. Med. Assoc.,* May 1, 1920.)

STABLE VITAMIN PRODUCT.—Dubin and Lewi prepared a stable vitamin product, designated, "V." An analysis shows the chief components to be calcium, expressed as calcium oxide, 10 per cent.; phosphorus, 15 per cent.; nitrogen, 3.5 per cent.; fat, 2.5 per cent.; iron, 0.3 per cent.; silicates 5.6 per cent.; moisture, 10 per cent. The remainder goes to make up the rest of the phytin molecule—the main constituent of the product—which is double calcium and magnesium compound of inosite phosphoric acid. Owing to the method of preparation and to the results of experiments with normal and polyneuritic pigeons, normal and scorbutic guinea-pigs and finally with children presenting evidence of malnutrition, marasmus and rickets—a marked acceleration in the rate of growth having been obtained, particularly in the children—it is established that the product contains antineuritic, antiscorbutic and antirachitic vitamins. It is felt by the authors that until such time as the vitamins shall have been isolated and their chemical composition determined, their vitamin preparation is an admirable substitute and may be used with confidence in such a manner as described by Voegtlin.

It is not intended as a substitute for any method of treatment nor is it meant to be used in infant feeding only. Rather it is intended to be a valuable aid whenever its use is indicated. At the same time, it should not be lost sight of that the diet must contain sufficient protein, fats, carbohydrates and mineral salts and that the caloric value must be adequate for the needs of the individual. (From *Amer. Jour. of Med. Sciences, Phila.;* through *Jour. Amer. Med. Assoc.*, May 29, 1920.)

CAUSES OF RANCIDITY OF COCONUT OIL.—Two-year storage tests were made by Perkins on thirty samples of edible coconut oil. The results were in general agreement with the accepted views of rancidity and its causes. The action of light was found to be a powerful, but not necessary, factor in the production of rancidity. Enzymes from the fresh coconut meat had some effect on the keeping qualities of the oil, but sterilization was of doubtful benefit. An oil of low initial acidity remained sweet during two years' exposure to air and light. The measurement of rancidity is discussed briefly. (From *Philippine Jour. of Science, Manila;* through *Jour. Amer. Med. Assoc.*, May 22, 1920.)

STERILIZATION OF DRINKING WATER.—Among the chemicals investigated by De Blasi he found silver fluoride most effectual, but it required a comparatively strong solution and contact of an hour to completely sterilize the water. The water is rendered limpid afterward by addition of sodium thiosulphate. Cattle and horses drink water containing up to 1 : 10,000 of the silver fluoride (*tachiolo*) without reluctance or apparent harm, he adds. His research with sodium hypochlorite and certain other chemicals merely confirms what others have published. (From *Annali d'Igiene, Rome;* through *Jour. Amer. Med. Assoc.*, May 22, 1920.)

RAPID METHOD FOR THE DETERMINATION OF SULPHUR IN PETROLEUM OILS.—A. W. Christie and C. S. Bisson (*J. Ind. and Eng. Chem.*, 12: 171–172, 1920).—After the combustion of 0.5 to 0.6 Gm. of the sample in a calorimetric bomb with oxygen under a pressure of 30 atmospheres for the determination of the calorific value, the whole of the sulphur present in the oil has been oxidized to sulphuric acid. The contents of the bomb are washed through filter-paper into a 250 Cc. beaker, and the total acidity of the liquid is determined by titration. The solution is then made up to a definite

volume such that an aliquot portion of 25 Cc. will contain between 0.2 and 1.5 Mgm. of sulphur. A portion of 25 Cc. is measured out into a 300 Cc. wide-mouthed conical flask and acidified with one drop of dilute hydrochloric acid; 10 Cc. of a solution of benzidine hydrochloride (8 Gm. per litre) are added, the solution is shaken several times and allowed to stand for fifteen minutes or longer. The benzidine sulphate is collected in a Gooch crucible on an asbestos pad which has previously been treated with permanganate. The flask is rinsed three times with 5 Cc. of cold water, each portion being drained through the filter before the next is poured on. The asbestos pad and precipitate are then washed back into the original flask. One Cc. of 10 per cent. sodium hydroxide is added and the flask is warmed on the steam bath to dissolve the benzidine sulphate. Water is then added to bring the volume up to about 100 Cc. and 5 Cc. of concentrated sulphuric acid are added. The flask is placed on the steam bath and the solution is titrated hot with $N/20$ permanganate until the red color fades slowly. An excess of 10 Cc. of permanganate is added, and heating on the steam-bath continued for exactly ten minutes. Ten Cc. of $N/20$ oxalic acid are added, and as soon as the solution clears the titration is finished off with permanganate. The net consumption of permanganate is multiplied by the factor 0.041 to obtain the number of Mgms. of sulphur in the portion of original solution taken, this factor having been ascertained by the analysis of known solutions of sulphates. The results are essentially the same as those obtained by the gravimetric barium sulphate method. By using the entire rinsings of the bomb and concentrating to 25 Cc., accurate results may be obtained for oils containing only 0.1 per cent. of sulphur.—J. F. B. (From *The Analyst*, May, 1920.)

Determination of Vitamine.—R. J. Williams (*J. Biol. Chem.*, 42: 259–265, 1920).—The author has previously shown that the anti-beri-beri vitamine is necessary for the nutrition of yeast (*J. Biol. Chem.*, 38: 456, 1919), and this fact has been adapted to the estimation of the amount of vitamine present in solution. The rate of growth of yeast and the number of cells produced from one cell under standard conditions in eighteen hours is directly proportional to the amount of vitamine present.

The microscopical method, although yielding good results, is troublesome, and the following gravimetric method, which yields

more accurate results, has been adopted: The culture solution is of the usual type, containing cane sugar, asparagine, and various salts in water; 100 Cc. of this solution are placed in a 500 Cc. flask, the solution to be tested added, and the whole diluted with water to 110 Cc. The flask is plugged with cotton-wool, sterilized, and cooled to 30° C.

A suspension of fresh pressed yeast is made containing 0.3 Gms. in 1 litre of sterile water, well shaken, and 1 Cc. is introduced into the culture medium with a sterile pipette. The flask is placed in an incubator at 30° C. for eighteen hours, and the growth is then stopped by the addition of a little formalin. The yeast is filtered off through a weighed Gooch crucible, washed with water and alcohol, dried at 103° C., and weighed. The increase in weight over that of a blank determination is directly proportional to the vitamine solution added. The "vitamine number" of a material is defined as the number of Mgms. of yeast produced by the addition of its extract computed to 1 Gm. of the original material tested.

A discussion of the method is given, in which it is shown that the vitamine to be tested must be in solution, that foreign organisms present in the yeast offer no serious handicap to the working of the method, and that the usual substances present in vitamine solutions do not accelerate the growth of the yeast. (From *The Analyst*, August, 1920.)

Critical Study of Methods for the Detection of Methyl Alcohol.—A. O. Gettler (*J. Biol. Chem.*, 42: 311–328, 1920).—The author has examined fifty-eight tests described in the literature by employing them with the distillates from a number of liquors to which known amounts of methyl alcohol were added ranging from nil to 30 per cent., in addition to five typical confiscated methyl alcohol liquors—a total of eighteen. The various reactions are divided into two groups: (A) Those in which the methyl alcohol must be oxidized to formaldehyde before testing, and (B) those in which the methyl alcohol is tested for directly.

On the whole, the former class yields more reliable and sensitive reactions, and is subdivided according to the class of compound with which the formaldehyde reacts—*e. g.*, phenylhydrazines, phenols, alkaloids, proteins, amines and miscellaneous substances.

The most satisfactory and sensitive reactions are: (*a*) Phenylhydrazine-ferric chloride-hydrochloric acid. (*b*) phenylhydrazine-

sodium nitroprusside-sodium hydroxide, (*c*) apomorphine-sulphuric acid, (*d*) peptone-ferric chloride, (*e*) reduced fuchsine-sulphuric acid and two crystal-producing tests, (*f*) *B*-naphthol-hydrochloric acid and (*g*) hexamethylenetetramine-mercuric chloride.

The five color reactions are sensitive to 1 in 200,000 but the crystal-forming reactions are reliable down to 5 per cent. of methyl alcohol and in solutions containing less than this amount the alcohol must be concentrated by fractional distillation.

Of the reactions classed under the heading of Group (B) only two out of twelve appear to be reliable and easily performed. These are: (*h*) boiling for seven hours with hydroxylamine and potassium hydroxide under a reflux condenser when cyanide is produced and may be tested for in the usual way and (*i*) determination of the sp. gr. and refractive index of the solution. The former test is very sensitive while the latter is reliable for not less than 5 per cent. of methyl alcohol and is liable to interference by the presence of substances other than ethyl and methyl alcohols and water.

Detection of methyl alcohol in liquors: 100 Cc. of the liquor are neutralized with sodium carbonate to phenolphthalein and slowly distilled until 50 Cc. of distillate are collected. This is divided into two portions of 30 Cc. and 20 Cc. the latter being tested directly by the above reactions (*h*) and (*i*). To the 30 Cc. portion of distillate 100 Cc. of 10 per cent. sulphuric acid are added followed by 6 grams of potassium dichromate and the whole allowed to stand ten minutes. The flask is connected to a condenser and distilled so that about 30 Cc. of distillate are collected in one hour. This distillate contains most of the acetaldehyde and is rejected and distillation then continued somewhat more rapidly until about 60 Cc. are obtained. This fraction which contains nearly all the formaldehyde is then tested by the above reactions in the following sequence: (*b*), (*c*), (*d*), (*e*), (*g*), (*f*). A definite reaction with one or two of these tests only may be due to foreign substances, but if methyl alcohol was originally present, all the results obtained will be positive.

Detection of methyl alcohol in tissues: 500 Gms. of tissue are finely ground and placed in a large distillation flask with 500 Cc. of water. Sulphuric acid is added until a distinctly acid reaction is produced, and the mixture is then distilled in a current of steam. Three hundred Cc. are collected, neutralized, and again distilled slowly, this distillate being oxidized as above, when subsequent

distillation gives all the formaldehyde in the first 40 Cc. The final distillate is then tested by the same reagents as given above under examination of liquors, omitting the hexamethylenetetramine-mercuric chloride test.

Full details are given for the preparation and employment of the various reagents, which are classed according to their reliability, sensitiveness, and ease of application. (From *The Analyst*, August, 1920.)

A Source of Error in the Sulphosalicylic Acid Test for Albumin in Urine.—Schall reports that sulphosalicylic acid when combined with urine containing large amounts of calcium produces a precipitate which so closely resembles albumin as to cause confusion. The precipitate is, however, denser than any sediment or other clinical findings. Control tests with other albumin reactions, heating, or previous dilution of the urine, serve to avoid diagnostic errors. (From *Munchener medizinische Wochenschrift*, Munich, February 6, 1920, 67, No. 6; through *Jour. Amer. Med. Assoc.*, August 28, 1920.)

Comparison of Recent Staining Procedures for Tubercle Bacilli.—Jötten and Haarmann commend their modification of the Spengler method for the demonstration of tubercle bacilli. After the smear has been stained in the usual manner with carbolfuchsin solution it is decolorized (twenty seconds) with a 15 per cent. nitric acid solution. It is then briefly rinsed and again treated for ten seconds with nitric acid; rinsed again and afterward counterstained for about thirty seconds in Spengler's picric acid-alcohol mixture (saturated aqueous picric acid and absolute alcohol, equal parts). The smear is again rinsed and allowed to dry and is now ready for microscopic study. Out of 170 sputum specimens the Ziehl-Neelsen method yielded fifty-nine positives and the Spengler original method gave sixty-one, whereas the modification just described furnished sixty-two positives. Furthermore, the average number of bacilli visible in the field was thirty-one for the modification, twenty-six for the Spengler original method and only thirteen by the Ziehl-Neelsen method. (From *Munchener medizinische Wochenschrift*, Munich, June 11, 1920, 67, No. 24; through *Jour. Amer. Med. Assoc.*, August 28, 1920.)

Purification of Benzoic Acid by Fractional Condensation.—Benzoic acid, made by the chlorination of toluene, is con-

taminated with small amounts of compounds chlorinated in the ring, the presence of which is most objectionable from the physiological point of view when benzoic acid is used in food products. While it is very difficult to remove these compounds by the ordinary methods of purification, benzoic acid practically free from chloro-derivatives was obtained in the Bureau of Chemistry by the use of a special apparatus. This apparatus consisted of a vessel in which the crude benzoic acid was placed. The vessel was immersed in an oil bath kept at a definite temperature. A blast of hot air was passed into the crude benzoic acid and the vapors coming off were conducted through a series of chambers, maintained at different temperatures. The least volatile chloro-derivatives separated out in the hotter chambers, whereas the more volatile benzoic acid collected in the colder chambers. (Max Phillips and H. D. Gibbs, *J. Ind. Eng. Chem.*, 12: 277 (1910); through *Jour. Franklin Institute*, May, 1920.)

ORIGIN OF PEPSIN.—Pavlovsky reports research which has apparently demonstrated the important share of the spleen in the formation of the gastric ferments, and that injections of spleen extract increase the quantity and improve the quality of the secretion in the stomach. Injections of fresh leukocytes and red corpuscles from the horse acted in the same way. All confirm the rôle of the spleen in normal digestion as well as in blood production, and sustain the principle that the secretion of an organ is perhaps the best stimulant to promote its secretory function. He gives the details of series of tests on dogs with a Pawlow gastric pouch, given an intramuscular injection of 25 Cc. of a 25 per cent. decoction of spleen tissue, the blood count recorded over long periods, and the units of gastric digestion. (From *Semana Medica*, Buenos Aires, Mar. 18, 1920, No. 12; through *Jour. Amer. Med. Assoc.*, Aug. 21, 1920.)

NEWS ITEMS AND PERSONAL NOTES.

A. D. M. A. RESOLUTIONS ON THE DECEASE OF RICHARD C. STOFER.—In testimony of the high regard it entertained for its late President, Mr. Richard C. Stofer, the American Drug Manufacturers' Association recently adopted the following resolution on his death:

"RESOLVED, That it is with profound sorrow that the American Drug Manufacturers' Association learns of the demise of its beloved

President, R. C. Stofer, and that, while it offers to the bereaved family a sympathy that an appreciation of his lovable qualities makes heartfelt, it likewise offers them the consolation that is to be found in the thought that their beloved husband and father still lives in the good works he has left behind him, and in the cherished memories that his sterling manhood has instilled in all who were fortunate enough to know him."

CINCINNATI COLLEGES AMALGAMATED.—The amalgamation of the Queen City and the Cincinnati Colleges of Pharmacy has been announced and the joint classes are being conducted in the building of the Cincinnati College of Pharmacy.

The Cincinnati College of Pharmacy was founded in 1895. The institution was conducted as a corporation for many years, but some years ago all the stock passed into the hands of Professor C. T. P. Fennel, son of Professor Adolph Fennel, one of the founders, who had been teaching in the institution for many years.

The Queen City College of Pharmacy was founded by Dr. Frank Cain in 1912 and became a part of Lebanon University two years later. When the charter of that institution was taken over by Wilmington College the control of the Queen City College was also taken over, and it has been conducted in Cincinnati as the school of Wilmington College since that time. Dr. Cain was succeeded as dean by Dr. Caswell A. Mayo, formerly of New York, and it was largely through his efforts that the amalgamation was effected.

With the coöperation of Professor Fennel, the Ohio Valley Druggists' Association has begun a campaign to raise sufficient funds to take over the College and to furnish a permanent endowment.

WOMEN PHARMACISTS AS TEACHERS.—Mrs. C. H. LaWall (Millicent S. Renshaw, P.D., P. C. P., 1904), is now Director of the Pharmacy Laboratory in the Women's Medical College of Philadelphia. Her assistant is Mrs. Mary Vogel, a recent graduate of the P. C. P. Formerly these positions were respectively held by Catherine G. Musson, P.D., P. C. P., 1901, who retired on account of ill health after 12 years of service in this position, and Bertha Whaland, P.D., 1906, M.D., 1911, who has opened a sanitarium at Bridgeton, New Jersey.

OBITUARY.

RICHARD C. STOFER.

In the decease of Mr. Richard C. Stofer, for fourteen years president of the Norwich Pharmacal Company, Norwich, N. Y., who died at the Norwich Memorial Hospital on September tenth after an illness of several months, another prominent figure among manufacturing pharmacists has passed away.

Mr Stofer was born September 11, 1862, in Wilmington, Delaware, and was educated in Philadelphia. In 1882 he entered the employ of Keasbey & Mattison Company, chemical manufacturers, of Ambler, Pennsylvania, leaving them in 1892 to become superintendent and chief chemist of the Norwich Pharmacal Company Later on he was made Vice-President, and in 1906 President; a position he held with honor to his company, and credit to himself, until his death.

During his twenty-eight years on the Norwich staff, he, more than any other one man, was instrumental in the growth of the house from a tiny business occupying a part of an old wooden piano factory, into a group of modern brick and concrete structures, containing many acres of floor space; from a concern comparatively unknown to one enjoying an enviable position among the half-dozen largest of its kind in the United States.

In local civic and philanthropic movements, he occupied a prominent place, serving from time to time as president or director of many organizations. He was also active in church and Masonic circles, a member of the American Chemical Society and of the American Pharmaceutical Association.

In the broader walks of pharmaceutical and industrial life, he was a figure of national prominence, filling, among many other offices, the dual rôle of President, for two years, of the American Drug Manufacturers' Association—an office regarded by many as the highest pharmaceutical honor in the United States—and as President of Associated Industries of New York State, made up of two thousand or more Empire State Industries, representing a capitalization of one and one-half billion dollars and a pay roll of ninety thousand employees.

Among the lesser offices to which he gave much of his energy and wisdom during the past few trying years, have been Director and Vice-President of the American Association of Pharmaceutical

Chemists, of which he was one of the founders, member of the executive committee of the National Drug Trades Conference, Director of the State Industrial Safety Council, member of the Advisory Council of the State Industrial Commission through appointment by Governor Whitman, member of the Council of National Defense, national counsellor to the United States Chamber of Commerce, etc.

He was always prominent in advancing uniform and just national drug legislation, preventing fradulent practices in the drug trade and in insuring just rewards of initiative, discovery and invention in the drug and chemical field. His natural qualifications fitted him to become a leader in the industrial world and his close study of conditions, his sympathetic comprehension of the other man's viewpoint, his unfailing geniality and his democratic, unassuming ways earned for him the respect and good will of leaders in industry everywhere.

By his own efforts he climbed to the pinnacle of his life's ambition, occupying not only a commanding position in the pharmaceutical world, but what was, to him, of far greater importance, *viz.*, enjoying the respect, confidence and esteem of a nation-wide circle of warm friends.

Mr. Stofer is survived by his wife and two children, a daughter, Helen, and a son, Dr. M. W. Stofer, who is Medical Director of the company to which his father gave the best years of his life.

BOOK REVIEWS.

"How to Pass the Board." By D. Chas. O'Connor. 435 pages. Published by the Spatula Publishing Co., Boston.

Any one, who has come in contact with numbers of applicants for registration by a State Board of Pharmacy, must realize the eagerness with which many of these applicants will hail the appearance of a book with such a title.

Approaching the work with the needs both of the examiner and of the applicant in mind, and finding that the author cautions the student against preparing only to pass the examinations and not for the future, the reviewer is inspired with the hope that here, at last, may be a book of this character more worthy than those heretofore available. But, alas, the hope is blasted by a more extended survey.

A book of this kind can hardly be expected to be an example of literary perfection. It should, however, conform to the common

rules of grammar and composition. It is difficult to conceive of a well educated author writing, "Do *not* study heavy subjects *neither* directly after a hearty meal. Several instances of this appear in the book. Also, contractions like couldn't, haven't aren't, etc., are scattered throughout the work. Misspelling is abundant. Much of it, no doubt, is due to faulty proof-reading, but, the fact that certain technical terms are repeatedly misspelled leads to the suspicion that it is a short-coming of the author, as well. Abbreviations are thickly sprinkled through the text. They are not always uniform. For instance, Potassium Iodide is abbreviated Pot. Iod. on one line and on the next Pt. Iod. Hydrochloric Acid is abbreviated by the use of the symbolic formula, H Cl, also given as H C L and even H. C. L. The last is the same as the currently used abbreviation for a prevalent economic condition. Such phrases as, "Lassar's Paste is a great seller in the big chain drug stores," occur with great frequency, are of no instructional value, and might well have been omitted in order to save space and avoid abbreviation.

Definitions are, in many cases, faulty. They should be more comprehensive. Destructive Distillation is defined as "the process of driving off the volatile portions from dry organic matter." According to this the sublimation of Benzoic Acid from Benzoin would be a process of Destructive Distillation. A Taenicide is stated to be a "medicine which kills worms," not being differentiated from a Vermicide, which is defined in the same words. In this connection it might be observed that faulty examples of definitions are frequently given. Chloral Hydrate is given as an example of a deliquescent substance. This flatly contradicts the statement of the Pharmacopoeia. In mentioning gums, the statement is made that "there are two official gums, Gum Camphor and Gum Arabic," a very unscientific grouping, and, at the same time, no mention is made of Tragacanth, which might be properly classed with Gum Arabic.

Chemistry, of all subjects, requires systematic treatment. There is, however, no attempt at a scientifically correct system of handling that subject.

The following are a few of the examples of inaccurate and misleading information distributed throughout the book:

"Dialyzed Iron is made by mixing a *solution* of Ferric Hydroxide with Ammonia Water," etc.

Narcotine is mentioned as a "Narcotic Principle."

Potassium Iodide is used in "Tincture of Iodine" to help dissolve the Iodine and *keep it from precipitating.*"

Boiling water is stated to be used to extract the Glycyrrhiza in making the Fluidextract. The official formula directs water and Ammonia Water.

Spirit of Camphor and others of this class are mentioned individually as "spirits."

The reasons for certain changes in official formulas, particularly in the N. F., are mere guess work, the logical reason being entirely overlooked.

"Caraway plant is a grain like wheat and oats."

"Lard is the fat from the hog's stomach."

Fluidextract of Malt is said to be official in the N. F.

"Rennin is the milk-curdling ferment of pancreatin."

"Colchicum is a small herb."

Saw Palmetto is described as "a shrub."

"Pomegranate is the dried stem and root."

Staphisagria is given as from a "larkspur tree."

Corn Silk is stated to have no official preparations, overlooking the Fluidextract.

Mucilage of Sassafras Pith is said to be used for dysentery and inflamed conditions of the stomach. The more important use as a delicate mucilage suitable for treatment of inflamed conditions of the eyes is ignored.

In discussing the treatment of strychnine poisoning, the statement is made that an "*emetic* of flaxseed tea, slippery elm tea is given."

A careful perusal of the book gives, at first, the impression that the author is a fairly well informed and efficient prescriptionist. Later, the conviction is borne home that he is woefully deficient in the thorough knowledge necessary to enable him to instruct and guide the type of student who will be most likely to use his book.

G. M. B., Jr.

LEGAL CHEMISTRY AND SCIENTIFIC CRIMINAL INVESTIGATION. By A. Lucas, F.I.C., Director Government Analytical Laboratory and Assay Office, Cairo. London, Edwin Arnold, 1920, pp. 181. Price, $3.40.

The author of this interesting book upon an important subject is apparently well qualified by experience and training to contribute authoritative data upon a number of phases of legal chemistry.

The collection of notes, for the author disclaims any pretensions to completeness as a treatise, covers an unusually wide and entertaining range of topics, as will be evidenced by the following list of chapter headings:

Alcoholic Liquors, Antiquities, Blood Stains, Building Materials, Bullets and Other Projectiles from Firearms, Clothing, Counterfeit Coins, Damage to Crops, Documents, Dust and Dirt, Explosives and Explosions, Fibres, Finger Prints, Fires, Firearms, Foods and Drugs, Gold and Silver Wares, Haschisch, Poisons, Pollution of Water by Sewage, Robbery from Letters and Parcels, Stains and Marks, Strong and Rope, Textile Fabrics, Tobacco, Traps for Criminals.

There is an introduction containing much valuable practical information and advice concerning the reception of the article, the records necessary to be made, the manner of reporting results and the facts bearing upon the subject in general.

Throughout the entire book the author has drawn upon the information available from his personal experience and quotes freely and interestingly from his case records. Some of the data and descriptions have a markedly oriental flavor as might be expected from an author whose experience has been largely gained in Egypt.

A valuable feature of the book is the bibliography to be found in connection with each monograph or chapter. While admittedly incomplete it nevertheless contains titles and references not often seen.

The author's style is facile and expressive. His material is entertaining, besides being valuable. Some of the monographs are as interesting as episodes in the career of the mythical Sherlock Holmes and the only fault one has to find with the book is that it is too brief.

It is a valuable contribution to forensic chemistry and will undoubtedly be consulted by many scientific experts for data not to be found elsewhere. C. H. LAW.

ANNUAL REPORTS OF THE CHEMICAL LABORATORY OF THE AMERICAN MEDICAL ASSOCIATION, Volume 12.—This is another valuable report emanating from the Chemical Laboratory of the American Medical Association. It again emphasizes the important functions of this adjunct to the A. M. A. established in 1906 and the value of the service rendered thereby.

The contents of this brochure of 112 pages is arranged in three

parts. Part I consists of reprints of a number of contributions from the Laboratory. Among these we consider of especial value the examinations of American-made synthetic drugs, such as procaine, barbital, holocaine, and cinchophen. In many of these the methods employed had to be original in the absence of official standards. The conclusions arrived at, "that American chemists were producing synthetic drugs formerly controlled by Germany and have thus declared their independence of German chemicals and from the evidence at hand the quality of American synthetics will be second to none," is indeed welcome and satisfying.

Part II contains reports abstracted from the *Journal of the A. M. A.* and from the Annual Reports of the Council on Pharmacy and Chemistry and these, as well as some of the articles in Part I, deal with the unwarranted and at times fraudulent claims made for proprietaries. These exposures should have a very salutary effect upon the practice of medication especially that of self-medication.

Part III contains reports not previously published. Among these important contributions we mention "Note on Melting Point of Acetylsalicylic Acid," "The Examination of Acriflavine and Proflavine," "The Examination of Commercial Barbital-Sodium," "The Examination of Luminal and Luminal-Sodium." Here also are given some additional reports upon proprietaries.

In each examination reported upon, the methods employed are reported in sufficient detail for the information of the chemist reader and the conclusions and deductions are set forth clearly. The methods employed at times are original and oft times ingenious and will prove valuable as suggestive to other analysts who have similar problems to cope with. G. M. B.

P-W-R MANUAL. Published by Powers-Weightman-Rosengarten Co., Manufacturing Chemists, Philadelphia, Pa.—This book of 471 pages, with its clear type, good paper and binding and with rounded corners to its pages is noteworthy and exhibits a practical application of the printers' art. The contents of this book evidence the highest ideals. It is a commendable effort on the part of a manufacturing corporation to impart accurate information concerning its products, standards of quality, and methods of testing. The clear, concise and scientific method of presentation of the subjects demonstrates the reliability of the work.

Above all the impartial manner of the statements appeals to us.

Despite the fact that it is a private publication covering commercial products of the publishers, there is a total absence of any attempt to advertise their business and contrary to the customary procedure in such "house publications" nowhere throughout the text occurs any reference to trade interests or even a suggestion that preference should be given to their products. We esteem it all the more highly because of this exceptional character and altruistic attitude.

The major portion of the book is devoted to monographs in alphabetical sequence and in style copying somewhat that of the U. S. P. but more condensed and at times more directly to the point. The International Atomic Weights for 1920 are given in tabular form, although the atomic weights of 1915 had been used in the preparation of the book. For all practical purposes this is immaterial. We note that in this table sulphur is spelled "sulfur," but we are happy to note that elsewhere throughout the book the official spelling of the U. S. P. is closely followed even to the dropping of the final "e" from such words as dextrin and glycerin and the retention of the final "e" in words ending in "ine," "ide," etc. In these monographs the official chemicals and standards are designated as U. S. P. and the standards for technical grades are stated separately.

In the Appendix are given a number of important tables and data commonly needed by analysts in the examination of the chemical products treated of in the book and these handy references will add very materially to the usefulness of the work. The closing chapter on Poisons and Their Antidotes is a practical and terse presentation of another subject that may require the attention of the pharmacist or chemist at any moment and the advice of the first sentence, "*The first thing to do in case of poisoning is to call for a physician,*" should be heeded.

In this exemplary publication, this manufacturing chemical house has compiled much valuable information and despite their modesty and self-obliteration the service they have thus performed merits commendation and should bring to them evidence of approval as well as continued material support. G. M. B.